THERMAL [1,5] SIGMATROPIC ALKYL SHIFTS OF 2,2-DIALKYLISOINDENES

By

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A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL
OF THE UNIVERSITY OF FLORIDA IN
PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1979

ACKNOWLEDGEMENTS

I wish to express my appreciation to Dr. William R. Dolbier, Jr, for his considerable assistance, chemical insight, patience, and encouragement during my years of doctoral research.

I also appreciate the help of the various support personnel in the chemistry department, and the technical assistance of Dr. Roy King.

There have been a good number of friends who have contributed to my positive experiences in Gainesville over the years. Special thanks go to Neil Weinstein for his help, and for being the inspiration behind so many good parties.

Lastly, I am grateful to my parents, who have been a major source of moral support, assistance, and encouragement in my quest for a Ph.D. degree.

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June 1979

Chairman: William R. Dolbier, Jr.
Major Department: Chemistry

Thermal [1,5] alkyl shifts were studied in the isoindene system for two purposes: to learn about the mechanism of the rearrangement and to determine relative migratory abilities of different alkyl groups in a [1,5] sigmatropic process.

Five novel benzobicyclic azoxy compounds were synthesized, for use as thermal precursors of 2,2-dialkylisoindenes. These 7-alkyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxides, in which the alkyl group was methyl, ethyl, isopropyl, cyclopropylcarbinyl, or benzyl, were made from 2-alkyl-2-methyl-1,3-indandiones via a four-step sequence. The key step was the last one, requiring the creation of a sequential hydrolysis-oxidation procedure.

The 2,2-dialkylisoindenes were generated as transient intermediates by the thermal extrusion of nitrous oxide at 180°C, in benzene solution. These isoindenes underwent facile [1,5] alkyl shifts under the reaction conditions, allowing the determination of relative migratory aptitudes for the following substituents: methyl:ethyl:isopropyl:cyclopropylcarbinyl:benzyl = 1:6.2:5.3:7.9:55.5.

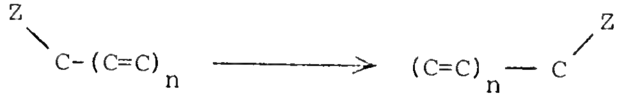
Isoindene intermediates were intercepted before rearrangement when the azoxy precursors were thermolyzed in the presence of dimethyl maleate or dimethyl fumarate. In each case, a single, stereospecific [4+2] cycloaddition product was formed between the isoindene and the dienophile.

Product studies of the thermolysis reactions, the use of a radical scavenger, and crossover experiments indicated that the [1,5] alkyl shifts were intramolecular processes, which did not involve fully-formed radicals. The migration results are consistent with a pericyclic mechanism, with the migrating group acquiring partial radical character in the transition state.

CHAPTER I
INTRODUCTION

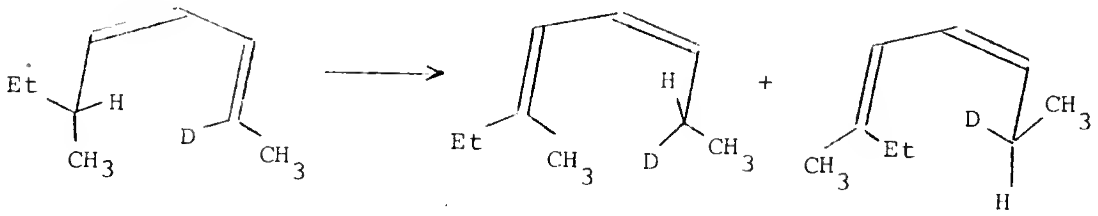
Thermal [1,5] Sigmatropic Reactions

A sigmatropic reaction consists of the concerted migration of a σ-bonded atom or group within the π-framework of an ene or a polyene. For a (1,5) sigmatropic rearrangement n=2, and the migration involves the π-electrons of two conjugated double bonds, resulting in the relocation of the π-bonds.



$$Z\text{-}C\text{-}(C{=}C)_n \longrightarrow (C{=}C)_n\text{—}C\text{-}Z$$

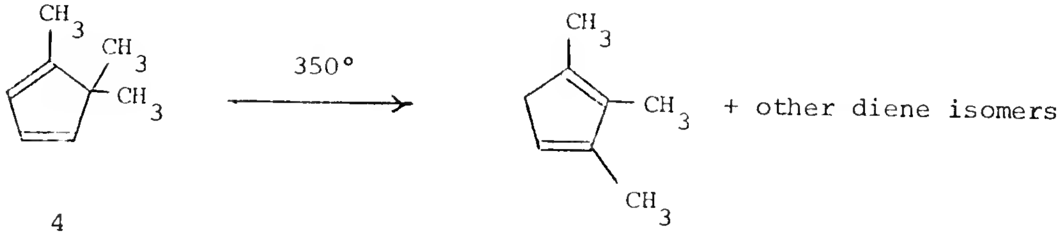
The Woodward-Hoffmann Rules predict that, in a thermal reaction, the [1,5] shift of hydrogen or an alkyl group will be a suprafacial process if a concerted pathway is followed.[1] The concerted, suprafacial nature of a (1,5) hydrogen shift has been demonstrated by Roth and Konig.[2] They showed that diene 1 rearranges in a completely stereospecific manner to give products 2 and 3.



1 2 3

Prior to the start of this work, there were relatively few reports of [1,5] sigmatropic alkyl migrations in the literature.[3] The investigation of thermal alkyl shifts had yielded little meaningful information about the reaction mechanism, due to two types of complications. Highly competitive [1,5] hydrogen shifts caused complicated product mixtures, or prevented formation of a stable product resulting solely from an alkyl migration. Also, a number of alkyl-shift processes exhibited more than one mechanistic pathway, involving an intermolecular component to the overall mechanism.

Various [1,5] shifts of alkyl groups had been observed only under relatively harsh thermal conditions. The [1,5] methyl migrations in 5,5-dimethylcyclopentadienes, such as 4, require an activation energy of 41-46 kcal/mole.[4-6] A temperature of 450°C is needed to rearrange the pentamethylcyclopentadiene 5.[7] A [1,5] methyl shift in 5,5-dimethylcyclohexa-1,3-diene (6) occurs only at or above 300°C.[8] On the other



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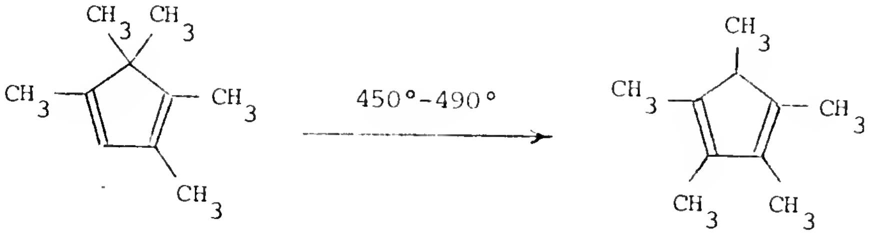

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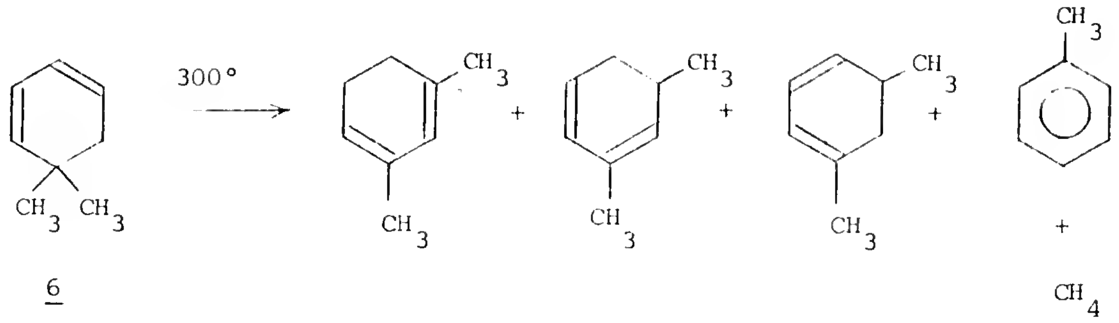
hand, a [1,5] hydrogen shift in the cyclopentadiene system (such as 7) requires an activation energy of only 20-23 kcal/mole, occurring at



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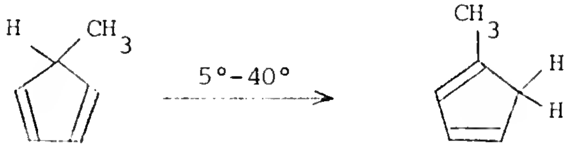
40°C.[9,10] Therefore, at the thermal conditions required for [1,5] alkyl migrations, one or more subsequent hydrogen shifts can readily occur, as in the rearrangements of 4 and 6.

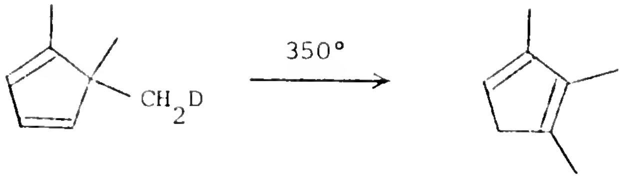


7

E_a = 20.4 kcal/mole

$\Delta S^{\ddagger} \simeq -10$eu

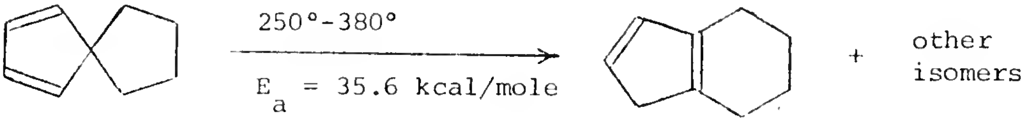
Concerted [1,5] sigmatropic methyl migrations were proposed to account for a number of rearrangements in cyclopentadienes, including spiro-annelated systems.[4-6,11,12] However, in a more recent study of 1,5,5-trimethylcyclopentadiene, using a deuterium on one methyl group (8), Willcott and Rathburn demonstrated that the methyl migration was, to a significant extent, an intermolecular process, involving a free radical chain pathway.[13] The 1,2,3-trimethylcyclopentadiene that was produced contained zero, one, two, or three deuterated methyl groups, indicating the exchange of methyl groups among molecules of 8 during the rearrangement. There is also evidence of a non-concerted, free radical component to the overall mechanism of [1,5] methyl rearrangement in 5,5-dimethylcyclohexa-1,3-diene (6).[8]



8

(d_0, d_1, d_2, and d_3 species)

While isomerizations of spirodienes, such as the spiro(4,4)nona-1,3-diene system (9), must be intramolecular processes,[11,12,14-17] the results of studies in the cyclopentadiene and cyclohexadiene systems raised the question as to whether any potentially intermolecular [1,5] alkyl shift process is indeed intramolecular. One goal of this research was, therefore, to find a thermal [1,5] sigmatropic alkyl rearrangement that proceeded solely by an intramolecular mechanism, even if an alternative free radical chain pathway is possible. Such a reaction could lead to useful mechanistic information about thermal alkyl shift processes.



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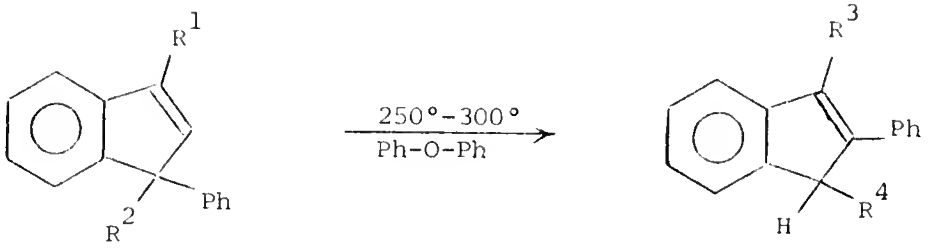
Relative Migratory Aptitude

The second goal of this project was to determine relative migratory aptitudes of a series of alkyl groups in a [1,5] sigmatropic reaction. No comparison of such rates had been made prior to this work on isoindene isomerizations. Relative migratory aptitude has been a useful probe in the mechanistic study of certain carbonium ion rearrangements, such as the pinacol rearrangement study of Bachmann and Ferguson.[18]

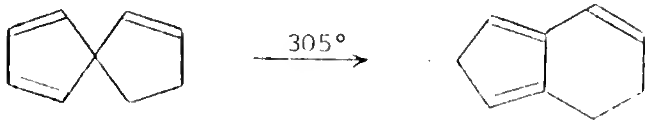
In a sigmatropic investigation, Miller and Boyer determined that phenyl underwent [1,5] migration slower than hydrogen but faster than methyl in the indene system 10a-d.[19] Improved transition state



10a:	$R^1 = R^2 = Ph$	(a)	$R^3 = R^4 = Ph$
10b:	$R^1 = H,\ R^2 = Ph$	(b)	$R^3 = Ph,\ R^4 = H$
10c:	$R^1 = H,\ R^2 = Me$	(c)	$R^3 = Me,\ R^4 = H$
10d:	$R^1 = Ph,\ R^2 = H$	(d)	$R^3 = Ph,\ R^4 = H$

bridging by the hydrogen s-orbital compared to the sp^2-orbital of a phenyl group or the sp^3-orbital of a methyl group was suggested to explain the order. The preference for phenyl migration over methyl may be due to the use of low-lying π-orbitals in the transition state for phenyl bridging, since such orbitals are not available to alkyl groups.

Semmelhack, Weller, Foos, and Clardy found rapid [1,5] vinyl migrations in the pyrolyses of spiro compounds 11 and 12.[16,17] The low activation barriers for these rearrangements compared to that for 9 are not easily accounted for by a simple [1,5] sigmatropic shift mechanism.

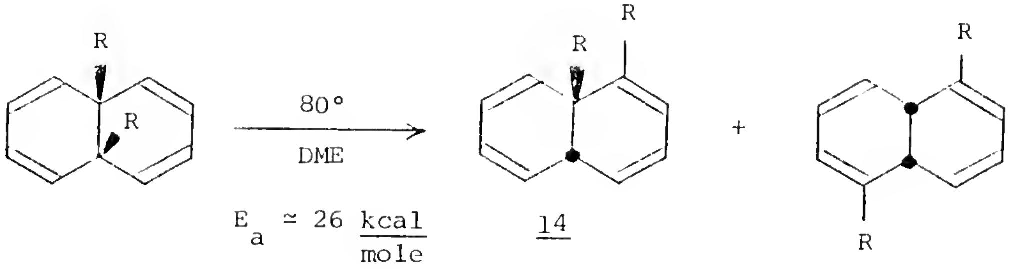


$E_a = 27.4$ kcal/mole

11

12

The authors favor transition states which involve the π-system at the migrating carbon for 11 and 12. The interaction of the lowest unoccupied molecular orbital (LUMO) of the migrating bridge with the highest occupied molecular orbital (HOMO) of the cyclopentadienyl π-system could stabilize these transition states, thereby explaining the faster [1,5] migration of vinyl or butadienyl bridges relative to saturated ones. Paquette and Carmody also discovered a facile [1,5] shift of a 1,3-butadienyl group in the rearrangement of tetraene 13 to isomer 14.[20] Alternative migration of a carbomethoxy or methyl group was not



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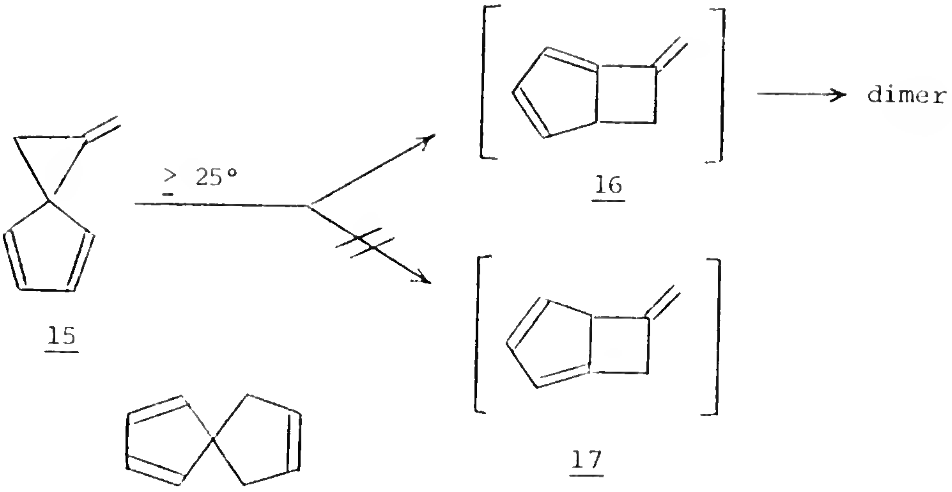
13a: R = Me

13b: R = CO_2Me

competitive, indicating that a vinyl carbon possesses inherently better latent migratory capability in this particular structural situation.

In another comparison of migratory aptitudes among hydrocarbon moieties, Miller, Kaufmann, and Mayerle observed that an allyl σ-bond migrated in preference to a vinyl one.[21] In an unprecedented low-temperature ring expansion, spirotriene 15 rearranged to isomer 16, with



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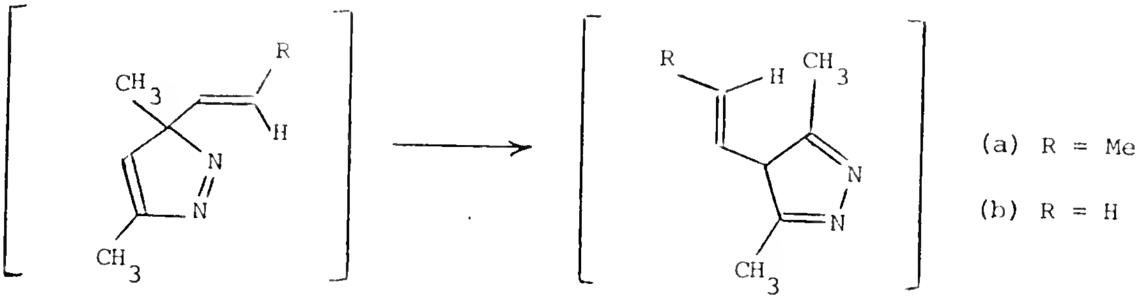
16

17

18

no formation of 17 observed. This migratory order contradicts Semmelhack's report that the allyl migration in spirotriene 18 is slower than the vinyl or butadienyl migrations in 11 or 12, respectively.[16] However, Epiotis and Shaik have suggested that, for [1,5] sigmatropic rearrangements in substituted cyclopentadienes, it is the group with the lowest ionization potential which preferentially migrates.[22] On this basis, allyl should migrate faster than vinyl.

In the study of rearrangements in heterocyclic compounds, Sharp and coworkers observed a thermal [1,5] vinyl shift that occurred in preference to a methyl migration in the intermediate 19.[23] In the pyrazoline system 20, McGreer and Wigfield determined that a carbomethoxy



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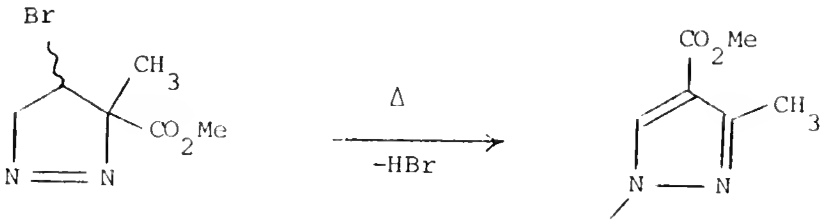
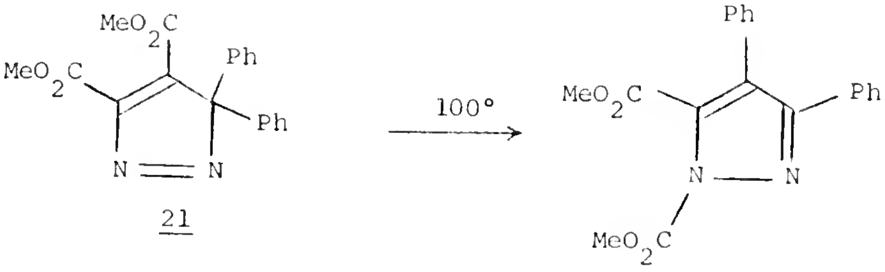
group migrates in preference to methyl.[24] In addition, a carbomethoxy group shifted faster than phenyl in pyrazole 21, according to Bramley



20

and coworkers.[25] However this observation is only relevant if a competitive [1,5] shift situation actually occurs during an intermediate step.



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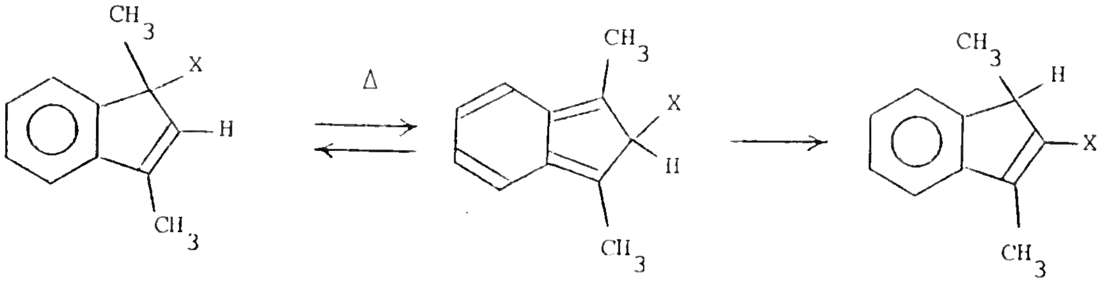
Relative migratory aptitudes for a variety of unsaturated groups in [1,5] sigmatropic reactions have been examined in recent years.[26-30] Studying racemization rates of indenes 22, Field, Jones, and Kneen concluded that substituent effects (of X) were in the order: $\mathrm{CHO} > \mathrm{COPh} \simeq \mathrm{COMe} > \mathrm{H} > \mathrm{CH{=}CH_2} > \mathrm{CONHMe} > \mathrm{CO_2Ph} > \mathrm{CO_2Me} > \mathrm{CN} \simeq \mathrm{C{\equiv}CH} > \text{alkyl}$.[30]



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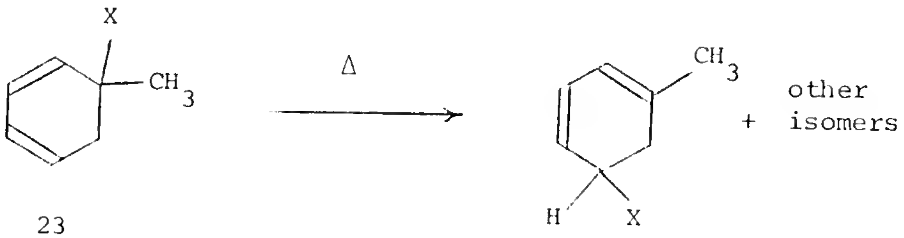
Similarly, Schiess and Funfschilling examined [1,5] sigmatropic shifts in the 5-methylcyclohexa-1,3-diene system (23) and found the following migration order: $CHO >> COCH_3 > H > CO_2 > CH_3$.[26, 31] The former workers

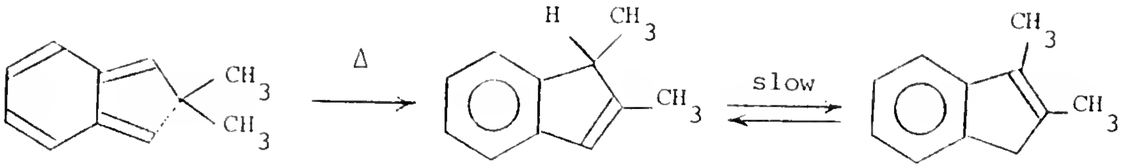


23

$X = H, CO_2CH_3, CHO, COCH_3$

rationalized their results in terms of a concerted migration involving an interaction of the HOMO of the diene system with the LUMO (π^*-orbital) of the migrating group. This conclusion was consistent with their more recent results, in which it was shown that electron-poor vinyl groups migrate faster than electron-rich vinyl groups.[29,30] The resonance electron-accepting ability of the migrating group was thought to be the determining factor.

Although the cyclopentadiene system was not useful for the determination of relative migratory abilities of alkyl groups in sigmatropic reactions, isoindenes such as 24a are well suited. Since a gain in aromaticity accompanies the [1,5] alkyl migration in going from 24a to the dialkylindene 25, the activation energy (and the required temperature) for this process is much lower than for a similar alkyl shift in cyclopentadienes. The subsequent hydrogen rearrangement yielding the isomeric indene 26 is slow relative to the process of interest: the conversion of 24a to 25. This is due to the loss of aromaticity that accompanies a [1,5] hydrogen shift in 25. Therefore, the sole or major product is that resulting from the alkyl shift itself.



24a

25

26

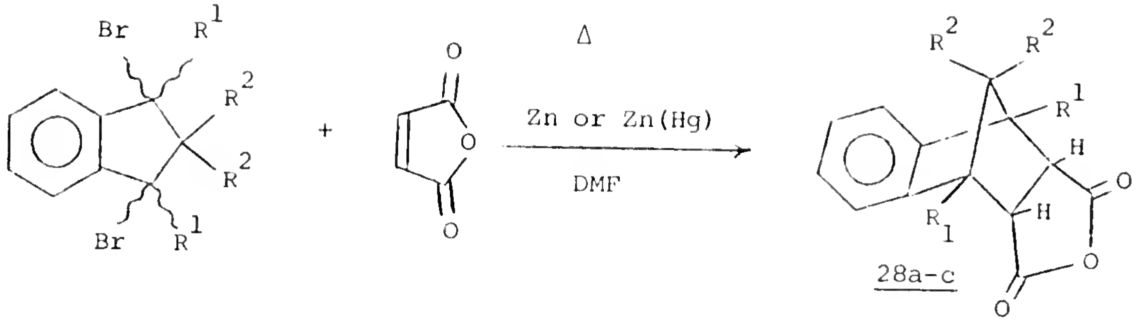
If two different alkyl groups are on the 2-position of the isoindene, the identity of the migrating group can easily be determined from the nuclear magnetic resonance (nmr) spectrum.

The use of 2,2-dialkyl-substituted isoindenes in this research provided the first unambiguous example of a thermal [1,5] sigmatropic alkyl shift that is totally an intramolecular process, despite having the potential to be intermolecular.

Isoindenes

Before the start of this work, 2,2-dialkyl-2H-indenes had never been isolated. (Hereafter, 2H-indenes will be called isoindenes.) However, a variety of isoindenes had been prepared as reactive intermediates, and trapped in [4+2] cycloaddition reactions with good Diels-Alder dienophiles.

In 1961, Alder and Fremery reacted the dibromoindanes 27a-c with zinc or zinc amalgam in the presence of maleic anhydride. Good yields of [4+2] anhydride adducts 28a-c were obtained, implying the existence of the isoindene intermediates 29a-c.[32] When 27a was debrominated in the absence of the trapping agent, a mixture of indene and polymer was obtained, and the parent isoindene 29a was believed to be the intermediate.

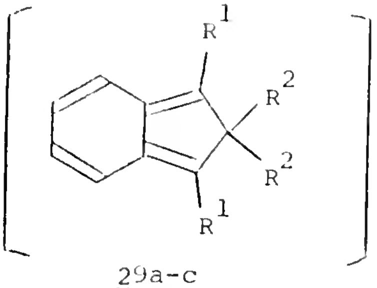


28a-c

27a: $R^1 = R^2 = H$

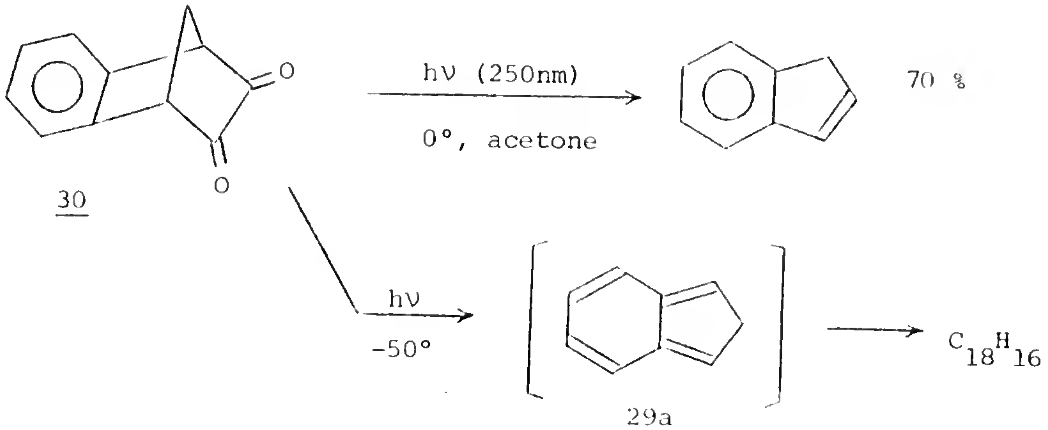
27b: $R^1 = H$, $R^2 = Me$

27c: $R^1 = Ph$, $R^2 = Me$



29a-c

Isoindene was also trapped by Warrener, Russell, and Lee during the photo-bisdecarbonylation of α-diketone 30.[33] Cycloadducts were obtained using N-methylmaleimide or dimethyl azodicarboxylate as the trapping reagent. In the absence of a dienophile, irradiation (250 nm) of 30 at 0°C led to indene as the major product. However, photolysis at -50°C yielded a dimer of the postulated isoindene intermediate.

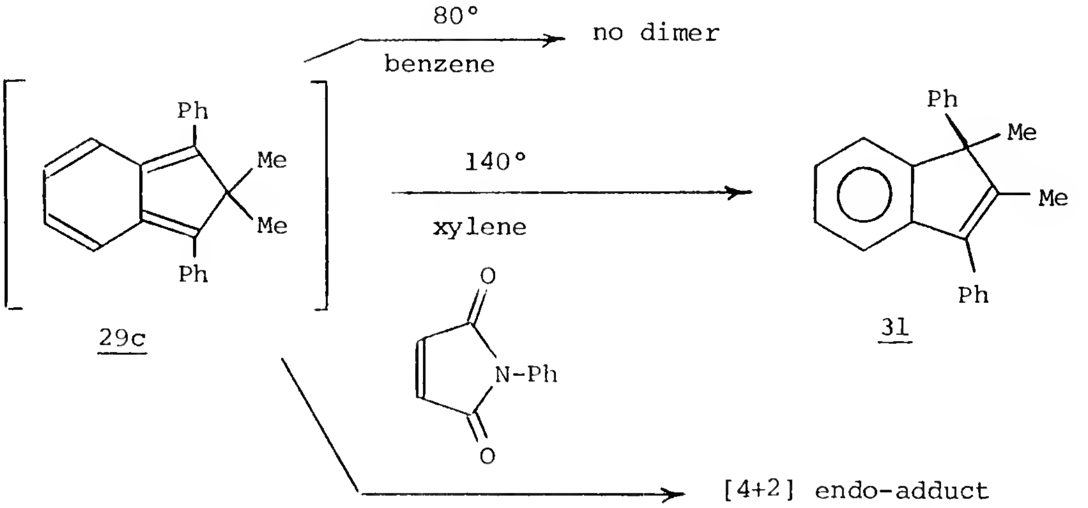


30

29a

$\mathbf{29a} \xrightarrow[X=Y]{h\nu}$ [4+2] adduct

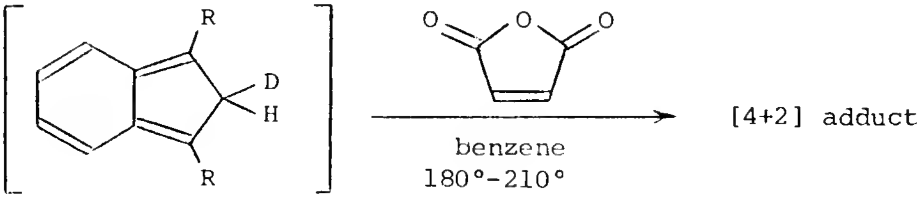
Holland and Jones treated dibromoindane 27c with copper powder in refluxing benzene, obtaining a stable solution of isoindene 29c in benzene.[34] The ultraviolet (uv) absorption spectrum of 29c exhibited a λ_{max} = 444 nm. No dimer was isolated when the benzene solution was refluxed for a long time, but if 29c was generated in xylene, boiling caused the yellow color to fade, and 1,2-dimethyl-1,3-diphenylindene (31) was isolated. In the presence of N-phenylmaleimide, the isoindene intermediate was trapped in a cycloaddition reaction.



29c

31

Berson and Aspelin used maleic anhydride to trap 1,2,3-trideutero-isoindene 32a during the thermolysis of 1,1,3-trideuteroindene at 180°C.[35] The 2-deutero intermediate 32b was intercepted in a similar manner by Isaacs, during the solution thermolysis of 2-deuteroindene.[36] In the latter case, the rate of disappearance of 2-deuteroindene varied with

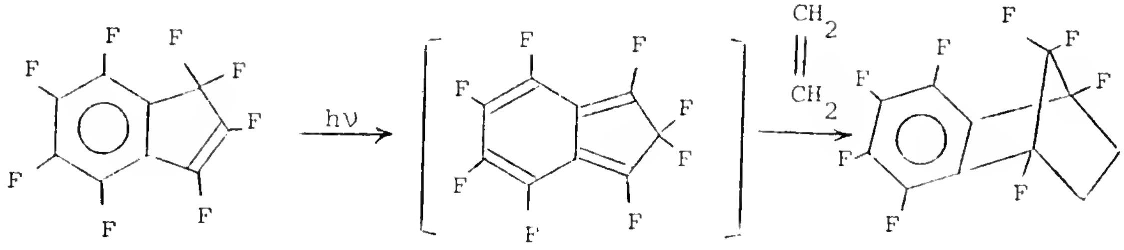


32a: R = D

32b: R = H

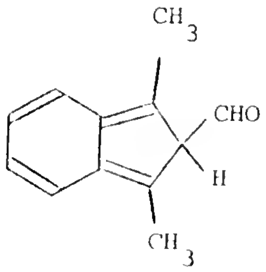
the concentration of maleic anhydride. A charge-transfer complex of maleic anhydride with the indene was suggested to best explain the observations.

Just prior to this dissertation work, Feast and Preston photolyzed perfluoroindene (33) in the gas phase, generating the perfluoroisoindene intermediate 34.[37] In the presence of ethylene, isoindene 34 was trapped as the [4+2] cycloaddition product 35.



33 34 35

In recent studies, Jones, Field, and Kneen intercepted the 2-formylisoindene intermediate 36 with N-phenylmaleimide;[27] De Fonseka and coworkers obtained a [4+2] cycloaddition product from 4-phenyl-1,2,4-triazoline-3,5-dione and 1,2,3-triphenylisoindene (37).[38] In the latter experiment, intermediate 37 was generated at -70°C from the photolysis of 1,1,3-triphenylindene. At the same temperature, nmr and uv spectra were obtained for solutions of 37 and 29c.



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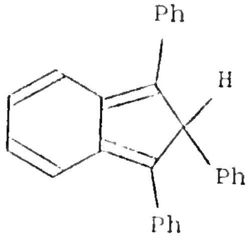
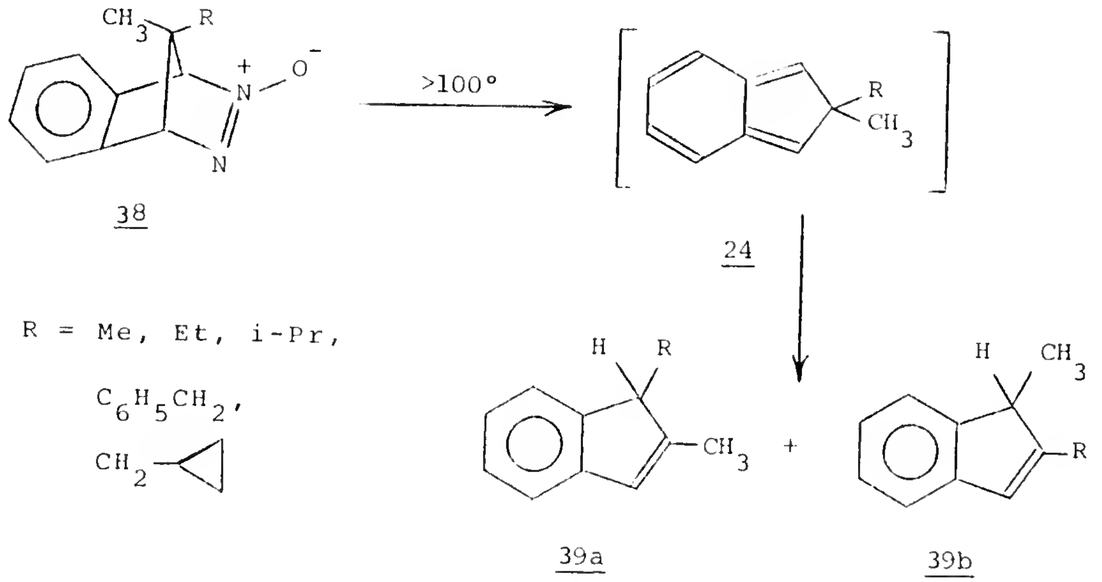


37

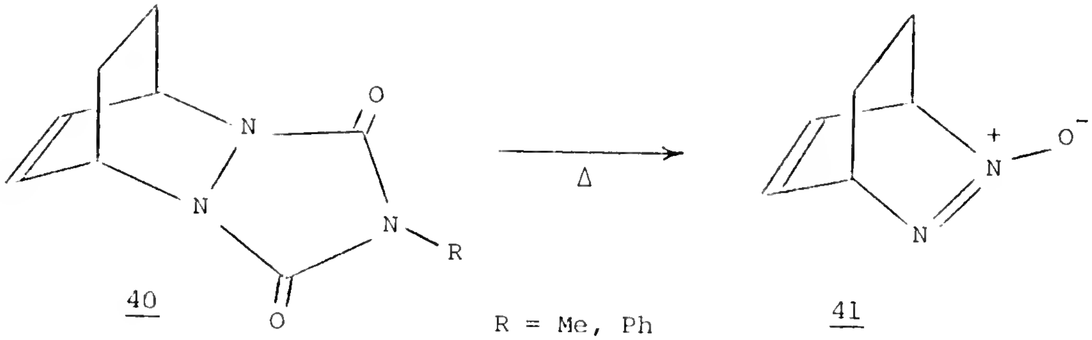
Since there was no evidence that 2,2-dialkylisoindenes could be isolated, at the time that this dissertation work was started, a decision was made to generate these species as transient intermediates during thermal reactions. The benzobicyclic azoxy compound 38, due to its expected thermal stability, was chosen as a suitable precursor of the dialkylisoindene system 24. The decomposition of 38, involving the extrusion of nitrous oxide (N_2O) via a [4+2] retrocycloaddition, was thought to require a temperature of more than 100°C. It was hoped that the isoindene intermediate (24) would undergo rapid [1,5] alkyl migration to yield the dialkylindenes 39a and 39b, avoiding the recognized, bimolecular reactions of isoindenes.[32,33]



Bicyclic Azoxy Compounds

It has been noted by Snyder that azoxy compounds are much more thermally stable than their azo counterparts, and that they seem to require about a 200° higher temperature to extrude nitrous oxide than is required by the analogous azo compounds to extrude nitrogen (N_2).[39] Since the azo system analogous to 38 was expected to lose nitrogen below room temperature,[40] the benzobicyclic azoxy molecule was a much more desirable precursor of the isoindene system 24.

Snyder and coworkers had previously prepared a number of bicyclic cis-azoxy compounds.[41] They reacted unsaturated hydrocarbons with 4-phenyl-1,2,4-triazoline-3,5-dione (or the 4-methyl derivative), obtaining such triazolinedione adducts as 40. Their bicyclic adducts would then be hydrolyzed and oxidized in one step, involving the simultaneous treatment of 40 with 30-35% hydrogen peroxide and excess potassium hydroxide, refluxing the reaction mixture in water or ethylene glycol-water solution. Azoxy compounds such as 41 were obtained in good to excellent yields (57-100%). Unfortunately, attempts to synthesize the benzobicyclic azoxy system (38) using a combination hydrolysis-oxidation procedure were not successful.

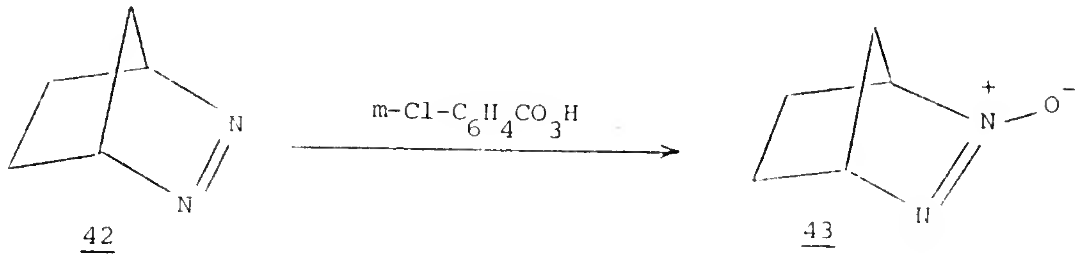


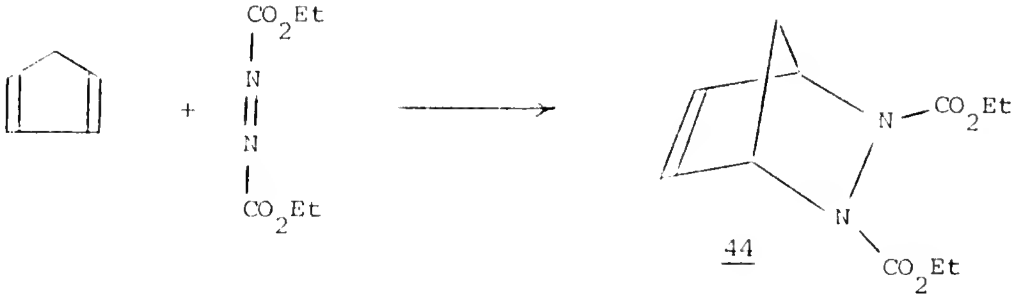
40

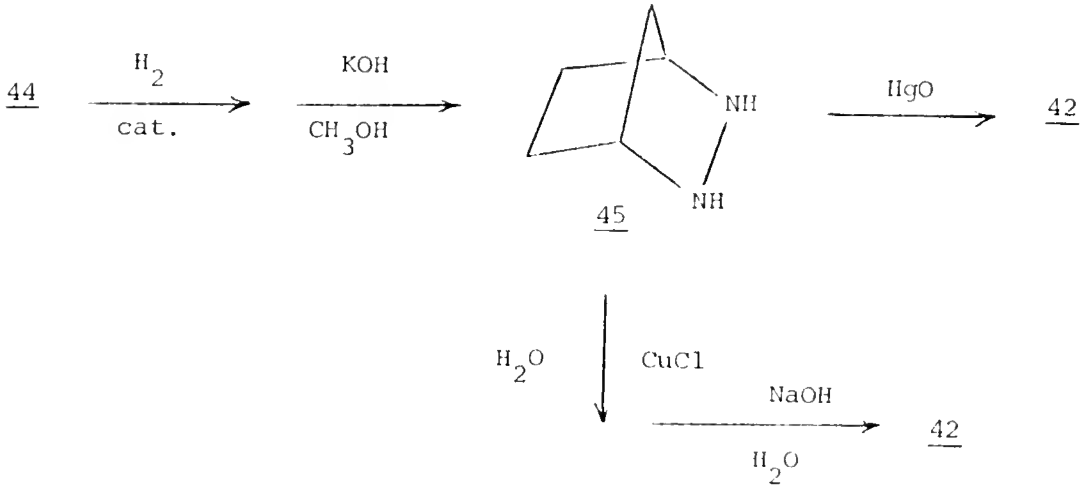
R = Me, Ph

41

Greene and Hecht oxidized the bicyclic azo compound 42 with meta-chloroperbenzoic acid, obtaining the cis-azoxy molecule 43 in 57% yield.[42] Azo compound 42 was prepared by the method of Diels, Blom, and Koll,[43] starting with the reaction of cyclopentadiene and diethyl azodicarboxylate to give the bicyclic Diels-Alder adduct 44. Catalytic hydrogenation of the double bond, followed by saponification of the ester groups, led to the hydrazo compound 45. Mercuric oxide was the preferred oxidizing agent for converting 45 into the azo compound 42, according to the procedural modification of Cohen, Zand, and Steel.[44] Attempts to prepare azoxy 38, or its azo analogue, using this type of synthetic route were unsuccessful. However, a diaza diester adduct similar to 44 was eventually employed as a successful precursor of the desired benzobicyclic azoxy compound 38.



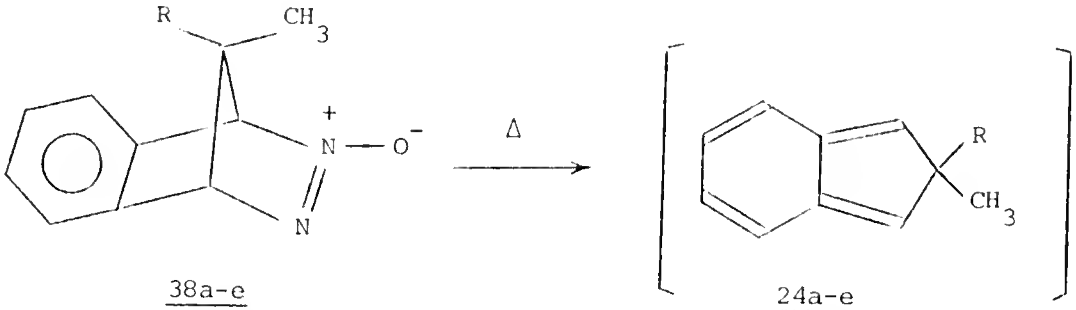




CHAPTER II
RESULTS

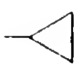
The Synthesis of Benzobicyclic Azoxy Compounds

Benzobicyclic azoxy compounds 38a-e, where R = methyl, ethyl, cyclopropylcarbinyl, isopropyl, and benzyl, were required as thermal precursors of the series of isoindenes 24a-e. A versatile, six-step procedure was designed and utilized in making the desired set of novel azoxy molecules.

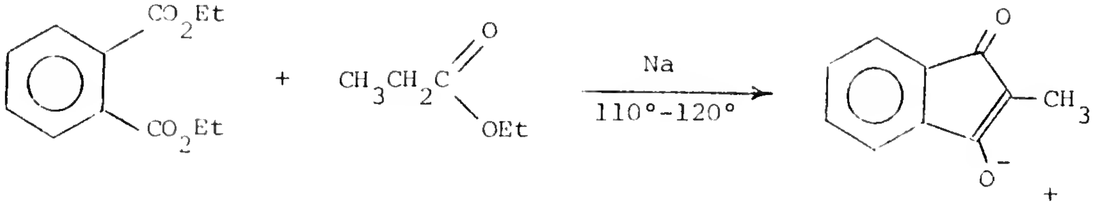


38a-e

24a-e

R = (a)Me, (b)Et, (c) CH_2  , (d)i-Pr, (e) $C_6H_5CH_2$

The same first step was used for all five of the azoxy compounds: the preparation of the sodium enolate of 2-methyl-1,3-indandione (46). Diethyl phthalate was reacted with ethyl propionate in the presence of powdered sodium, at 110°-120°C, according to the method of Wislicenus and Kotzle.[45] A crude, dark red solid was obtained and used without purification. In most cases, the sodium enolate could be alkylated directly (step 2) without complications, yielding the 2-alkyl-2-methyl-1,3-indandiones 47a-c and 47e. Methyl iodide, ethyl iodide, cyclopropylcarbinyl bromide,[46] and benzyl bromide served as the respective alkylating reagents, each being heated in ethanol solution with 46. The overall yields, through the first two steps, were 79%, 20%, 22%, and 34%,



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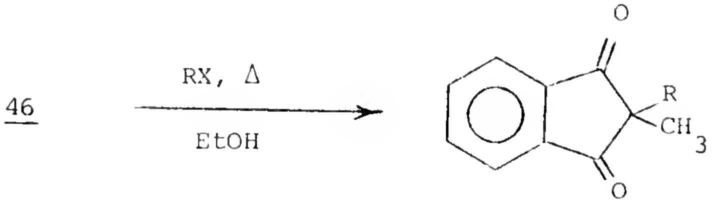
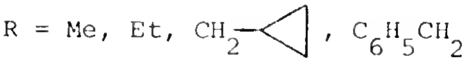
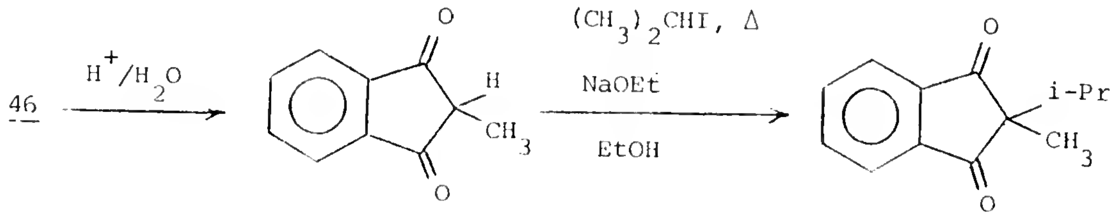


47a-c, e



for the indandiones 47a-c and 47e, respectively. Since it was difficult to separate 2-isopropyl-2-methyl-1,3-indandione (47d) from the unreacted diethyl phthalate (which was mixed in with the crude enolate 46), a different alkylation procedure was employed in making 47d. Modifying the method of Wislicenus and Kotzle,[45] 46 was protonated in acidic aqueous solution to give 2-methyl-1,3-indandione (48) in 21% yield. Purified 48 was dissolved in ethanol, and then heated in a sealed pyrex tube with isopropyl iodide and freshly prepared sodium ethoxide. Using this modification of the procedure of Aebi and coworkers,[47] dione 47d was obtained in 44% yield.



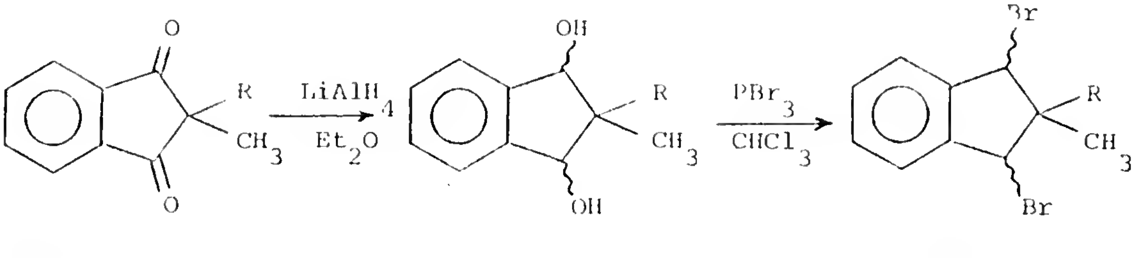
48

47d

The indandiones 47a, 47b, 47d, 47e, and 48 are known compounds whose physical properties have been published.[45,47-50] Indandiones 47c and 47e (containing a cyclopropylcarbinyl and a benzyl substituent, respectively) have two strong, sharp infrared (ir) bands in close proximity, at 1740 and 1710 cm^{-1}. This doublet pattern is typical for carbonyl stretching in indandiones.

The nmr spectrum of 47c exhibits a five-proton multiplet in the δ0.00-0.50 range for the cyclopropyl group. The nmr of 47e has two distinct aromatic hydrogen absorptions, including a five-proton singlet at δ6.89, indicative of the phenyl hydrogens of the benzyl substituent.

Synthetic steps 3 and 4 involved standard reactions for reduction and bromination, following the procedure of Alder and Fremery for making 1,3-dibromo-2,2-dimethylindane (27b).[32] The indandiones 47a-e were treated with lithium aluminum hydride to give the corresponding 2-alkyl-2-methyl-1,3-indandiols (49a-e) in 70-100% crude yields. A mixture of diol stereoisomers was obtained for each dialkyl-substituted system, but there was no need to separate the components. The diols 49a-e were then transformed into the corresponding 1,3-dibromo-2-alkyl-2-methylindanes (50a-e), using phosphorus tribromide. The yields ranged from 84-99%, except in the case of 50c (the cyclopropylcarbinyl derivative), which could only be made in 46% yield. The key feature in the ir spectrum



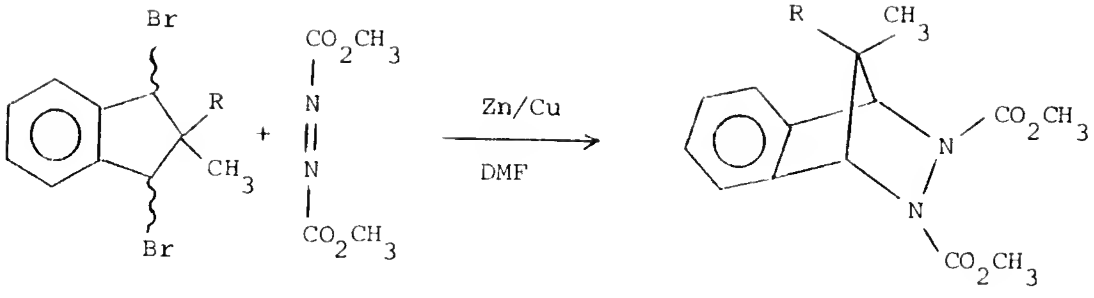
47a-e 49a-e 50a-e

of each indandiol is a strong, broad absorption band around 3310-3350 cm^{-1}, due to the stretching vibration of the O-H bond. A common characteristic of the nmr spectra of diols 49a-e is a multiplet in the δ4.15-5.20 range, assigned as the two benzylic protons, on the carbons bearing the hydroxy groups. The two hydroxy protons generally absorb as a broad singlet, somewhere between δ1.74 and 2.73.

The dibromoindanes 50a-e show a weak or moderate intensity ir band for the C-Br stretching vibration, located in the 530-600 cm^{-1} range. A common element of their nmr spectra is the multiplet in the δ5.00-5.50 region, due to the absorption of the two benzylic hydrogens, on the carbons bearing the bromine atoms.

The last two steps of the synthetic scheme involved replacing the bromine atoms with an azo N-oxide (azoxy) bridge across ring positions 1 and 3 of the indane skeleton, creating a benzobicyclic molecule. The dibromoindanes 50a-e were allowed to react with dimethyl azodicarboxylate in the presence of freshly prepared zinc-copper couple.[51] This caused the loss of both bromines, which was followed, in situ, by a cycloaddition reaction involving the azo compound. Diaza diester adducts 51a-e resulted, and the yields of these dimethyl-7-alkyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylates ranged from 86% to 94%.

In general, diesters 51a-e exhibited two overlapping infrared bands of strong intensity, at about 1710 and 1750 cm^{-1}. The two carbonyl groups, though identical, seemingly interact to cause the doublet pattern. The six carbomethoxy protons absorb as a singlet near δ3.70 in the nmr spectra of adducts 51a-c, whereas the corresponding signal is a doublet (around δ3.74) for diesters 51d and 51e.

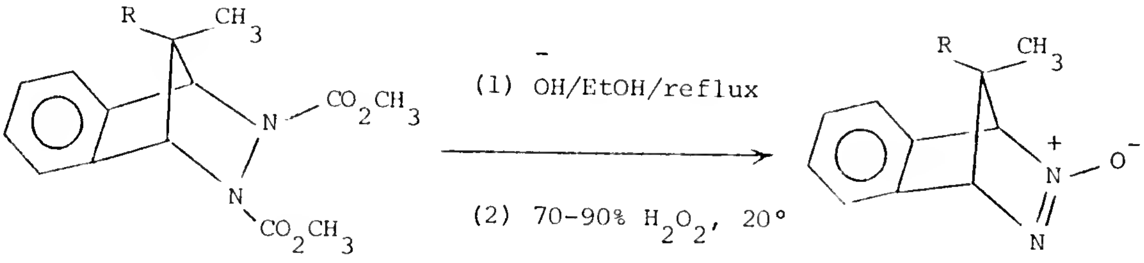


50a-e

51a-e

Though the two bridgehead hydrogens absorb as a broad singlet near δ4.95 for adducts 51a and 51b, compounds 51c-e show a two-proton multiplet in the δ4.84-5.27 region.

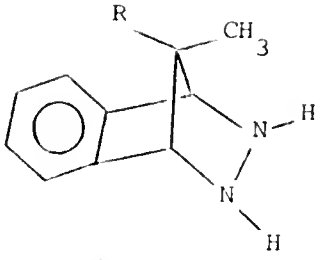
Conversion of the diaza diester adducts (51a-e) into the corresponding azoxy compounds (38a-e) was accomplished by a sequential hydrolysis-oxidation procedure. Using a custom-made reaction vessel and a vibromixer, each diaza diester was refluxed in ethanol solution with excess potassium hydroxide, under an argon atmosphere. The carbomethoxy groups



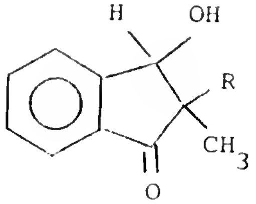
51a-e

38a-e

were hydrolyzed and removed, resulting in the presumed hydrazine intermediate 52. After cooling the reaction mixture to 20°C, 70-90% hydrogen peroxide was slowly added to form the 7-alkyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxides (38a-e). Two features of



<u>52</u>



<u>53</u>

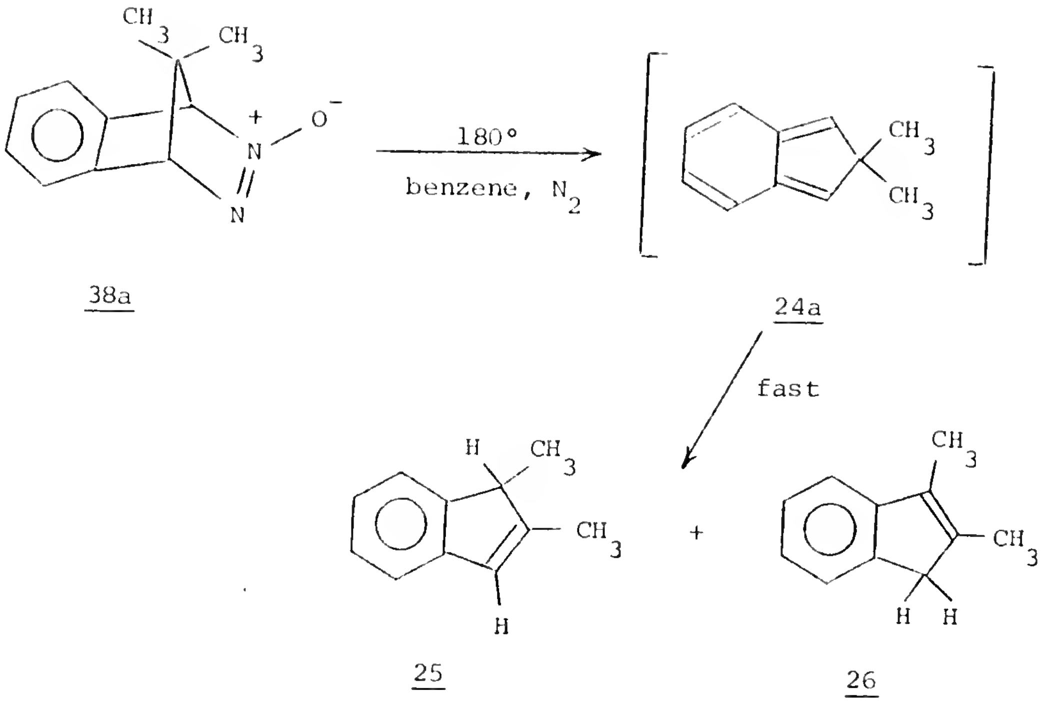
this procedure proved to be essential for the successful synthesis of the benzannelated azoxy compounds. First, the vibro-mixer,[52] which is an agitator that utilizes a vertical vibrating motion, was found to be indispensable. It was particularly effective in dispersing the heterogenous mixture that developed during the oxidation step, due to the partial insolubility of the organic species in the reaction medium. Secondly, the oxidation procedure, in all cases, had to be carried out as a separate step, and at a temperature not exceeding 25°C. Since the oxidation of <u>52</u> was quite exothermic, the hydrogen peroxide had to be added very slowly.

The major side product of each oxidation reaction was the corresponding keto alcohol <u>53</u> (shown above), which probably formed via decomposition of an intermediate azo compound to an isoindene (<u>24</u>). Approximately equal amounts of keto alcohol and azoxy compound were formed, and separation was effected by column chromatography. Final purification by trituration gave the azoxy compounds (<u>38a-e</u>) in 22-29% yield.

The most distinctive spectral characteristic of these azoxy compounds is a very strong infrared band at about 1510 cm^{-1}, due to the N=N stretching vibration. In general, the two bridgehead hydrogens show an nmr absorption within the δ4.90-5.50 region, as two small sets of peaks or multiplets. The nmr analysis of 38b, which possesses an ethyl and a methyl group, indicates a binary mixture of the 7-position epimers. Approximately 75% of the azoxy mixture appears to have the configuration shown previously (for R = ethyl), with the minor epimer having the ethyl group on the opposite side, over the azoxy bridge. The methyl substituent appears to absorb in two places in the spectrum: a large singlet at δ1.37 and a much smaller one at δ0.77 (the peak area ratio is about 3:1). The larger peak has the same chemical shift as the more downfield methyl singlet of the dimethyl azoxy compound (38a), and is believed to be the signal of a methyl group occupying the 7-position closer to the azoxy function. The smaller peak has about the same chemical shift as the more upfield methyl singlet in the nmr of 38a, and it represents a methyl occupying the position closer to the top of the benzene ring.

Product Studies of Thermolysis Reactions

The thermolysis of the dimethyl azoxy compound (38a) was carried out in benzene solution, heated in sealed pyrex tubes, under a nitrogen atmosphere. A 0.05M solution of 38a in benzene had to be heated above 175° in order to cause azoxy decomposition at a significant rate. At 180°, azoxy 38a exhibited a half-life of approximately 40 min, as it extruded nitrous oxide via a [4+2] cycloreversion process. The transient 2,2-dimethylisoindene (24a) thus generated underwent, in situ, a smooth [1,5] methyl migration to form almost exclusively 1,2-dimethylindene (25). A small amount of 2,3-dimethylindene (26) was also produced.



38a

24a

25

26

A series of thermolyses were performed on 0.05M solutions of azoxy 38a in benzene, with the following variations in reaction conditions: the temperatures were either 180° or 204°, and the reaction times ranged from 0.5 hr to 3.0 hr (refer to Table 1). The major product of each solution thermolysis was 1,2-dimethylindene (25), which forms via a [1,5] methyl shift in isoindene 24a. The relative amount of the minor product, 26, increased either when the temperature was raised to 204° or when the heating time exceeded an hour. The formation of 26 from isoindene 24a involves both a [1,5] methyl migration and the relocation of one hydrogen atom. The combined product yields (ca. 80%), as determined by gas chromatography (glpc), were found to be insensitive to changes in temperature (180°-204°), concentration (0.02-0.08M), and reaction time (0.5-3.0 hr). Since no other products were observed using this method of isoindene generation, such alternative isoindene reactions as dimerization, oligomerization, and polymerization were apparently not competitive with the [1,5] methyl migration.

Table 1

Thermolyses of Azoxy Compound 38a

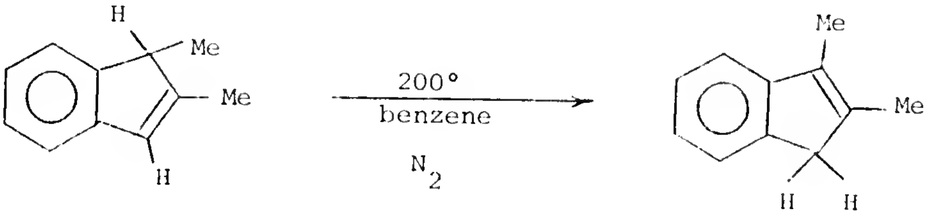
Phase	Temp (°C)	Time (hr)	Ratio of 25:26	Yield*
benzene (0.05M)	180	0.5	>50	82%
benzene (0.05M)	180	3.0	19	79%
benzene (0.05M)	204	0.5	8.5	82%
benzene (0.05M)	204	1.33	1.9	78%
cumene (0.05M)	180	3.0	10	79%
gas	350	flow system	0.5	

*The percent yields refer to the combined weights of indenes 25 and 26 obtained, with the theoretical yields based on the amount of azoxy 38a that decomposed.

Indenes 25 and 26 were purified by glpc, and easily distinguished by their nmr spectra. The former product shows two single-proton absorptions: a narrow multiplet near δ6.35 for the vinyl hydrogen, and a quartet at δ3.14 for the methine hydrogen, which is spin-spin coupled to the adjacent methyl group. In contrast, 26 exhibits a somewhat broadened two-proton singlet at δ3.15, due to its benzylic methylene group. The two methyl groups of 25 have separate signals: a doublet at δ1.26 for the 1-methyl substituent, and a singlet at δ2.04 for the methyl group on the vinyl carbon. On the other hand, the similar methyl environments of 26 give rise to a six-proton singlet at δ2.01. All of the nmr absorptions of 25 and 26 are consistent with the published spectral data of 1,2-dimethylindene and 2,3-dimethylindene, respectively.[53-56]

In one experiment, cumene was used as the thermolysis solvent instead of benzene, in order to see whether the presence of a good radical scavenger inhibited the rearrangement. The results were basically unchanged from the reactions in benzene, with essentially the same product yield. A gas-phase pyrolysis was also tried, heating 38a in a flow system to approximately 350° at a pressure of 0.15-0.20 mm. The same two dialkylindene isomers were formed, but hydrogen shifting was a more competitive process under this set of conditions. For, 2,3-dimethylindene (26) was the major product, with a 25:26 ratio of 0.5. Since a maximum value of this ratio was sought, where the major or sole product would be that resulting from only a [1,5] methyl shift (25), all of the following rearrangement studies were performed in benzene solution.

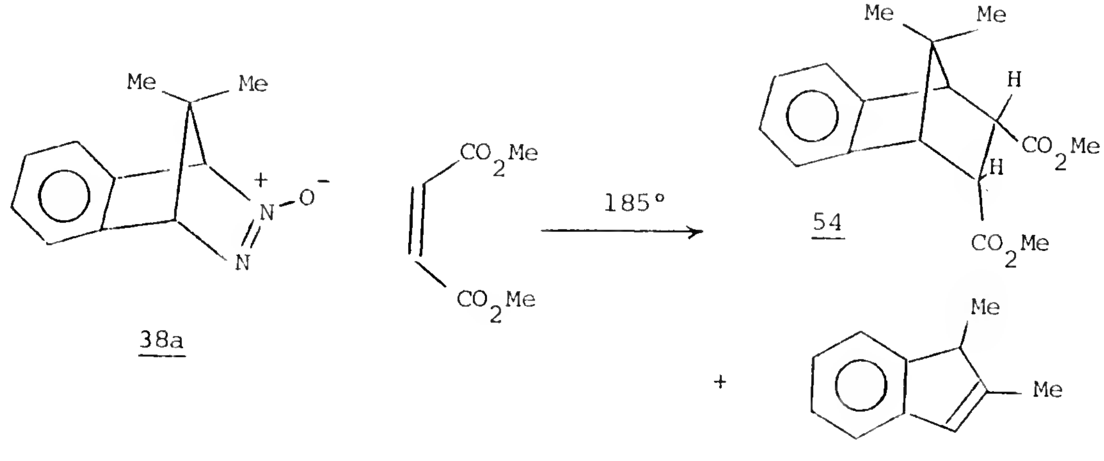
The thermolysis data were consistent with the formation of indene 26 from isomer 25. A pure sample of 1,2-dimethylindene (25) was thermolyzed at 200° for 24 hr, converting about 90% of the starting material into 2,3-dimethylindene (26), with no other products observed. Isomer 26 is more thermodynamically stable than 25, since the olefinic double bond of 26 bears one more alkyl substituent. This factor provides the driving force for the gradual rearrangement.



25

26

It was necessary to demonstrate that dimethylisoindene 24a was actually generated during the thermolysis of azoxy 38a. By trapping the isoindene intermediate, one could rule out a concerted transformation of 38a to indene 25. When the dimethyl azoxy compound (38a) was heated to 185° in benzene with an equimolar amount of dimethyl maleate, 75% of the product mixture was adduct 54, resulting from the [4+2] cycloaddition between dimethylisoindene 24a and the dienophile. The other 25% was 1,2-dimethylindene (25). When an 8-fold excess of dimethyl maleate was thermolyzed with this azoxy compound, 93% of the dimethylisoindene was trapped as 54 before methyl migration occurred, and only 7% of the product mixture was indene 25. With larger excesses of dienophile, essentially all of the sigmatropic process could be quenched.



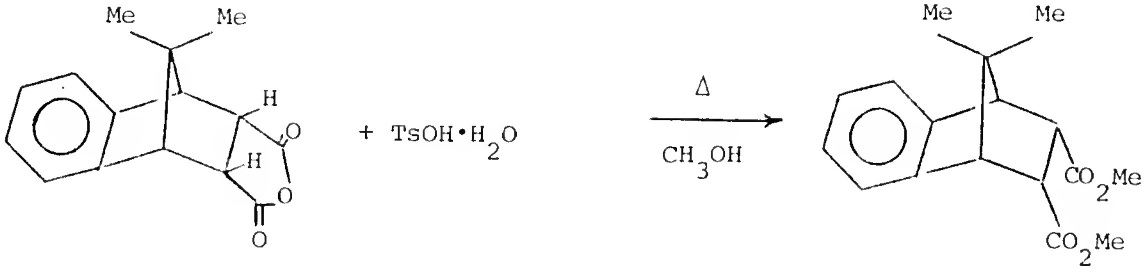
38a

54

25

The bimolecular trapping reactions involving dimethyl maleate were stereospecific, yielding only the cis-adduct with both ester groups in the endo position. The stereochemical configuration of 54 was determined from its nmr spectrum, which has a simpler pattern than that of the corresponding trans-diester adduct. First, the carbomethoxy groups are in identical environments, and their hydrogens exhibit a six-proton singlet at δ3.35. Secondly, there are two pairs of identical methine hydrogens: one identical pair at the bridgeheads, and the other adjacent to the ester groups. Each pair absorbs as a narrow two-proton multiplet within the 2.90-3.70 region.

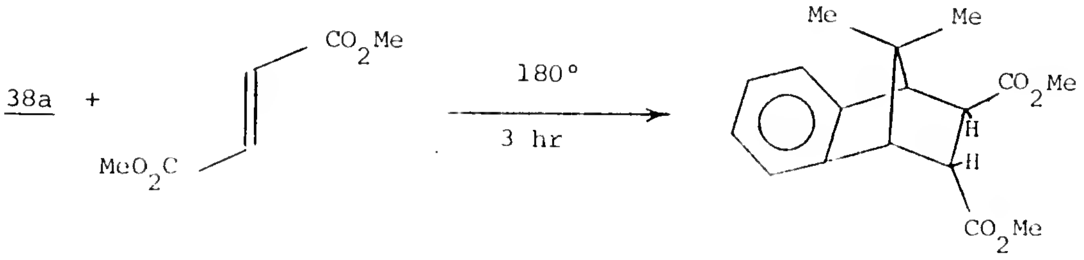
The endo-cis structure of the Diels-Alder adduct 54 was confirmed by authentic synthesis. The endo maleic anhydride adduct 28b, made according to the procedure of Alder and Fremery,[32] was refluxed in methanol with a catalytic amount of p-toluenesulfonic acid. The sole product was the endo-cis diester, identical in physical and spectral properties to 54.



28b

54

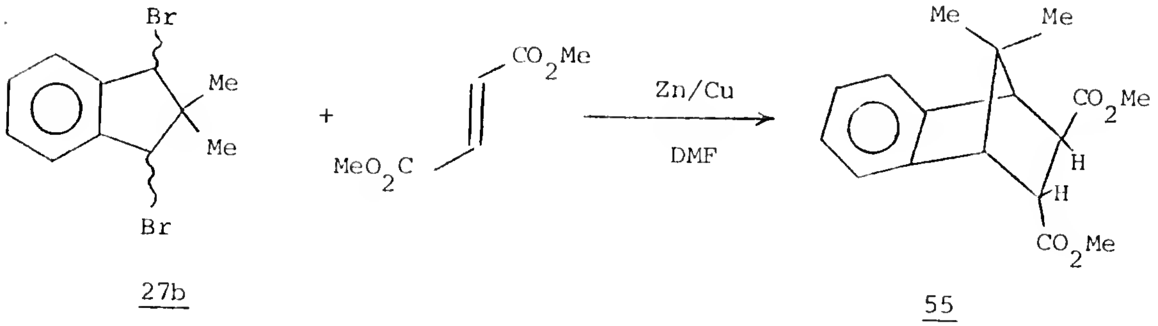
The 2,2-dimethylisoindene generated from the thermolysis of azoxy 38a was also trapped in a stereospecific reaction with dimethyl fumarate, forming as the only cycloadduct the trans-diester 55. A small amount of the primary rearrangement product, 1,2-dimethylindene (25), was also formed, along with a trace of 2,3-dimethylindene (26). Using a 1:1 ratio



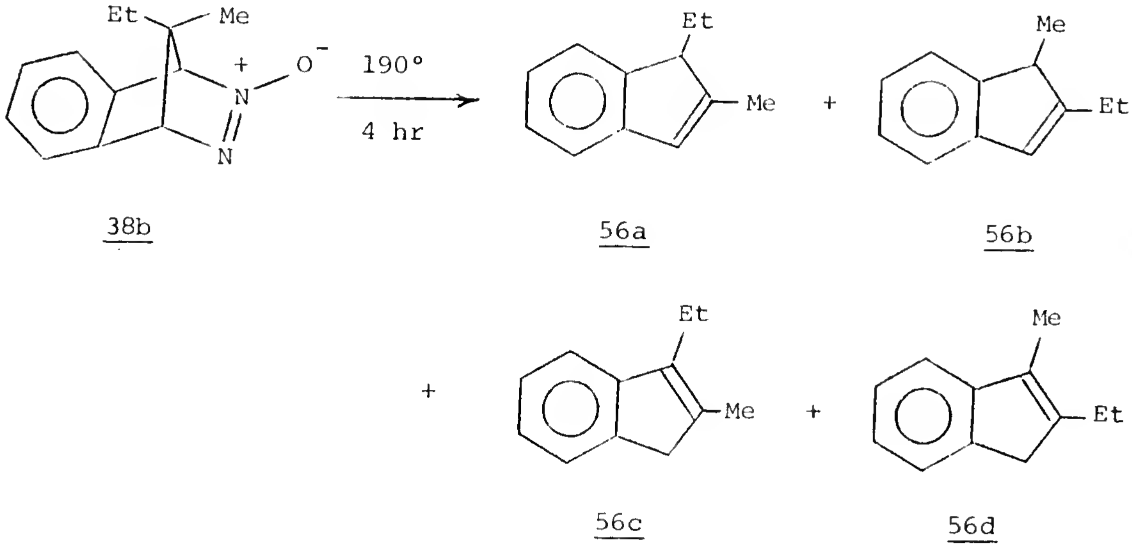
55

of dienophile to azoxy compound, the molar amount of cycloadduct (55) in the product mixture was 76%.

The trans-diester configuration was assigned on the basis of its nmr spectrum, since all four of the methine hydrogens should have different chemical shift environments, as well as the methyl hydrogens of the two ester groups. There are two carbomethoxy singlets in the δ3.40-3.90 region, and each of the methine hydrogens has its own signal, in the form of a little doublet or multiplet, within the range δ2.70-4.00. Confirmation of the trans configuration was gained by a comparison of physical properties with the same compound made by an alternate synthetic method. The dibromoindane 27b was treated with dimethyl fumarate in the presence of zinc-copper couple to give a trans-diester adduct that was identical to 55.



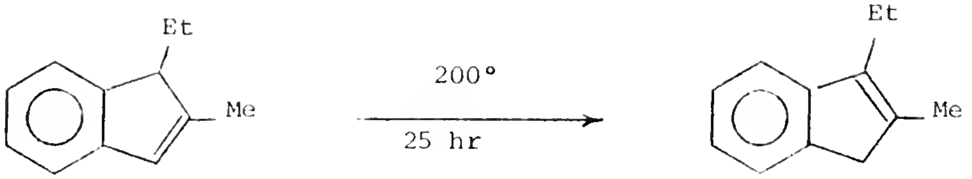
The ethyl, methyl-azoxy compound 38b was thermolyzed a number of times in benzene. The reactions were performed in pyrex tubes, which were sealed either at atmospheric pressure under nitrogen, or with a degassed solution under vacuum. The choice of sealing methods did not affect the experimental results. On the average, thermolyses were run at 190° for 4 hr, decomposing almost all of azoxy 38b. Under these conditions, the product mixture essentially consisted of four isomeric indenes having a molecular weight of 158: 1-ethyl-2-methylindene (56a), 1-methyl-2-ethylindene (56b), 2-methyl-3-ethylindene (56c), and 2-ethyl-3-methylindene (56d). A very small glpc peak (less than 0.2% of the sum of all peak areas) represented the only other component observed. This substance was not isolated, though it had the same retention time as 1,2-dimethylindene. The total product yield for the average thermolysis was 91%, based on the amount of azoxy 38b that reacted.



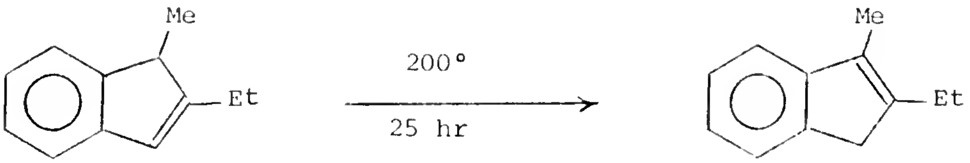
Isomer 56a was formed in the largest amount, typically constituting about 70% of the product mixture. Under milder thermolysis conditions (such as 190° for 2.0 hr, or 187° for 3.2 hr), significantly less of the azoxy compound decomposed. The product distribution also changed, as the percentages of 56a and 56b in the product mixture were increased relative to those of 56c and 56d. On the other hand, a higher thermolysis temperature (200°) caused all of the azoxy compound to react, and relatively more of the product mixture consisted of 56c and 56d than for the mixture obtained from the average (190° for 4 hr) thermolysis. When 38b was heated for 24 hr at 200°, more than 75% of the resultant indenes were 56c and 56d.

The nmr spectra of indenes 56a-d provided most of the information for the assignment of their structures. Only 56a and 56b have a vinyl hydrogen, which in each case absorbs as a narrow multiplet around $\delta 6.40$. The methine hydrogens on both isomers absorb near $\delta 3.20$, as a triplet in 56a and as a quartet for 56b. Instead of having single-proton absorptions, indenes 56c and 56d both exhibit a two-proton singlet at about $\delta 3.25$, due to their benzylic methylene groups. Indene 56a is the only isomer having an upfield signal between $\delta 0.00$-0.95: a triplet at $\delta 0.60$ for the CH_3 hydrogens of the ethyl group. For 56b, the two sets of methyl hydrogens have overlapping signals, creating a six-proton multiplet between $\delta 0.97$ and 1.42. Also, the methylene hydrogens of 56b are only spin-spin coupled with the CH_3 protons of the ethyl substituent, and absorb as a quartet at $\delta 2.37$. The nmr data of 1-ethyl-2-methylindene, 1-methyl-2-ethylindene, and 2-methyl-3-ethylindene have been published by other researchers, and they correlate well with the spectra of 56a, 56b, and 56c, respectively.[54,55]

Since the nmr spectra of isomers 56c and 56d are very similar, the best evidence for their structures came from the following isomerization reactions. When purified 56a was thermolyzed in benzene at 200° for 25 hr, about 90% of it reacted, forming as the sole product an isomer that was identical to 56c. The thermolysis of 56b under the same conditions caused approximately 80% of it to isomerize, and the single product was equivalent to indene 56d. The infrared data, particularly in the fingerprint region (between 7 and 11 microns), was very useful in determining the equivalency of dialkylindene products from different reactions. Since the reaction conditions in the above two thermolyses were expected to cause only hydrogen migrations in 56a and 56b,[19,30,57]



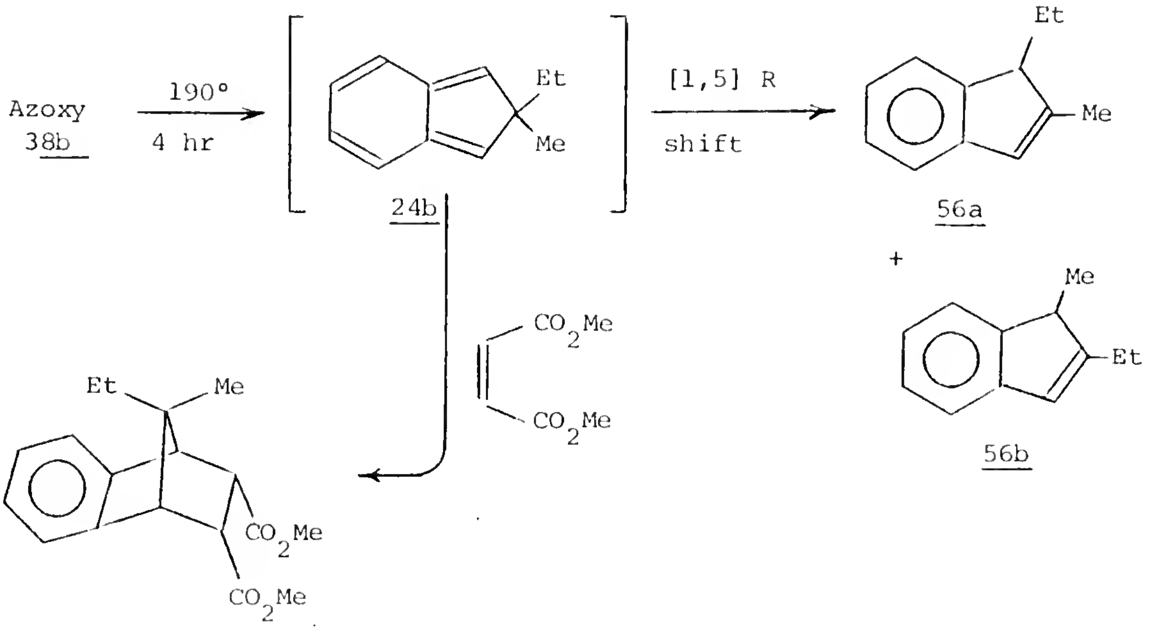
56a 56c



56b 56d

it follows that isomer 56c has the ethyl group in the 3-position, and that indene 56d contains a 2-ethyl substituent.

The existence of 2-ethyl-2-methylisoindene (24b) as an intermediate during the thermolysis of azoxy 38b was demonstrated by a trapping experiment. A 75-fold excess of dimethyl maleate was dissolved in a benzene solution of 38b, and the reaction was performed at 190° for

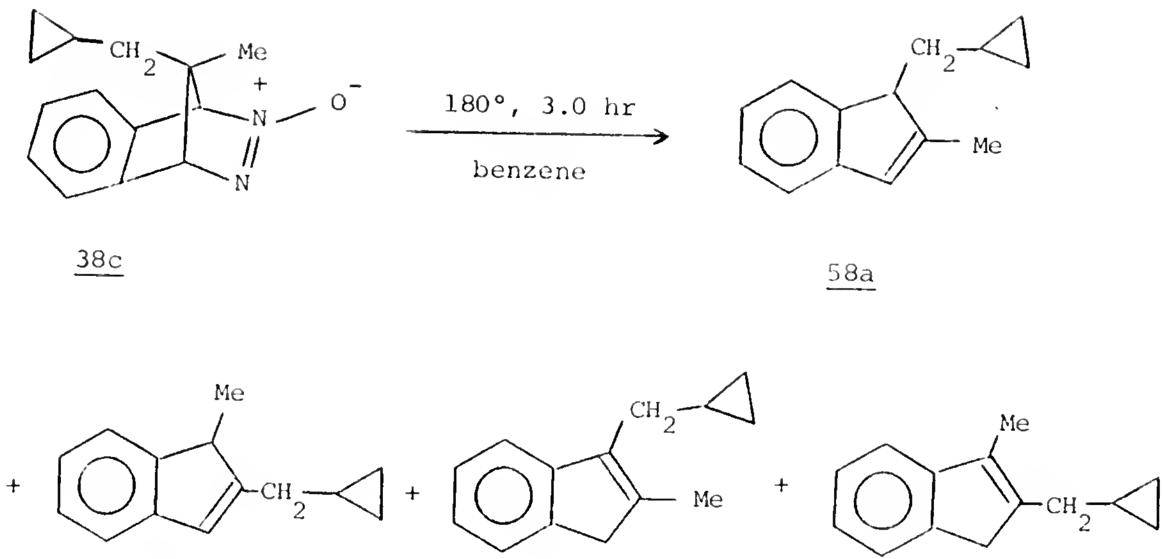


57

4.0 hr. The major component (73%) of the product mixture was the endo-cis diester adduct 57, which resulted from the [4+2] cycloaddition between isoindene 24b and the dienophile. The rest of the product mixture consisted of the alkyl rearrangement products, indenes 56a and 56b.

Adduct 57 shows strong, overlapping ir bands in the carbonyl stretching frequency region, at 1730 and 1755 cm^{-1}. The endo-cis diester configuration of 57 was assigned on the basis of its nmr spectrum, compairing it with the spectra of the dimethyl cis- and trans-diester adducts 54 and 55, respectively. Adduct 57 exhibits a tall, six-proton singlet at $\delta 3.47$ for the two equivalent sets of carbomethoxy hydrogens. In addition, there are just two narrow multiplets nearby, due to the two pairs of equivalent methine hydrogens. These two-proton multiplets, which have chemical shifts very similar to those of the corresponding signals in 54, occur in the following ranges: $\delta 3.04$-3.24, and $\delta 3.57$-3.82.

Azoxy compound 38c, containing cyclopropylcarbinyl and methyl substituents, was heated in benzene at 180° for 3.0 hr. Reactions were always carried out in sealed pyrex tubes, under a nitrogen atmosphere. Under this set of conditions, all of the azoxy compound decomposed. Every product mixture contained four isomeric indenes, having a molecular weight of 184: 1-cyclopropylcarbinyl-2-methylindene (58a), 1-methyl-2-cyclopropylcarbinylindene (58b), 2-methyl-3-cyclopropylcarbinylindene (58c), and 2-cyclopropylcarbinyl-3-methylindene (58d).



38c

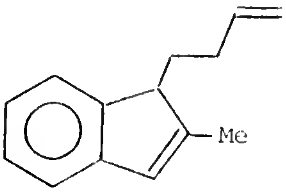
58a

58b

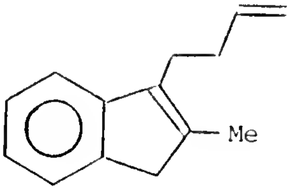
58c

58d

In order to determine whether the cyclopropylcarbinyl group was opening on some molecules to form a 3-butenyl group during the thermolysis, the product mixture was compared with authentic samples of 1-(3-butenyl)-2-methylindene (59) and 2-methyl-3-(3-butenyl)indene (60).

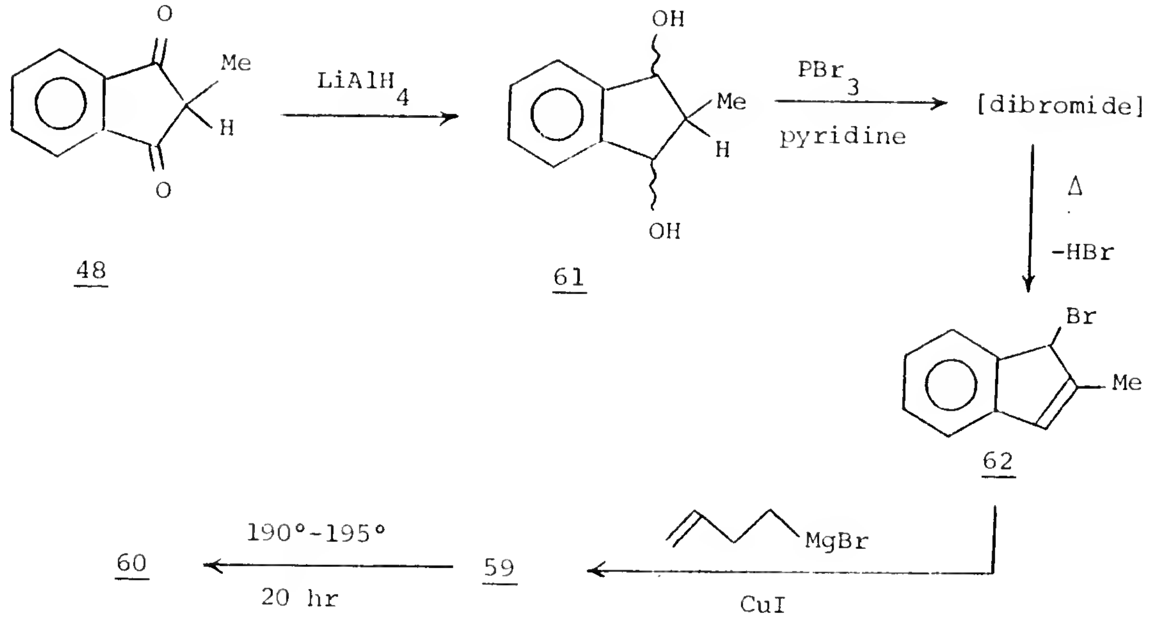


59



60

Indene 59 was prepared from 2-methyl-1,3-indandione (48) via a three-step synthesis. The dione was reduced with lithium aluminum hydride to form 2-methyl-1,3-indandiol (61) in 58% yield. This diol was treated with phosphorus tribromide and pyridine to give the corresponding dibromoindane, which dehydrobrominated upon distillation. The isolated product was 1-bromo-2-methylindene (62). The last step involved the reaction of 62 with 3-butenylmagnesium bromide, in the presence of cuprous iodide. This substitution of a 3-butenyl group for bromine yielded indene 59. Indene 60, the isomer of 59, was formed by heating the latter in benzene at 190-195° for 20 hr.

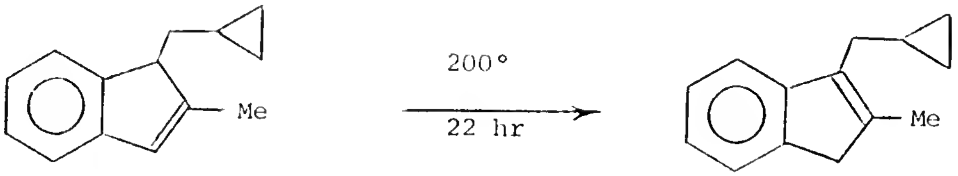


The butenyl-substituted indenes 59 and 60 were compared on a gas chromatograph with the product mixture resulting from the thermolysis of azoxy 38c. The analysis indicated that the product mixture consisted only of the four cyclopropylcarbinyl-substituted indenes 58a-d, with no evidence of cyclopropane ring-opening isomerization during the thermolysis. A quantitative yield of isomers 58a-d was obtained, and 86% of the product mixture was 58a.

A common characteristic of the nmr spectra of the four products is a very high-field multiplet in the δ0.08-0.80 region, due to the cyclopropyl hydrogens. However, the spectra easily differentiate the 1,2-dialkylindenes from the 2,3-dialkylindene products. Only the former (58a and 58b) have a vinyl hydrogen, giving both isomers a one-proton singlet near δ6.50. In addition, these two products have only one-proton signals around δ3.35, due to the benzylic methine hydrogen on each.

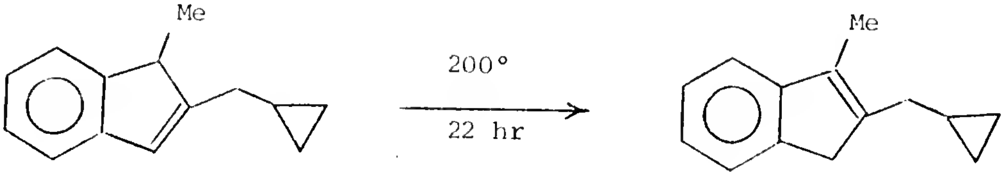
For 58a, this methine absorption is a triplet, and the corresponding signal of 58b is a quartet. On the other hand, the 2,3-disubstituted indenes, 58c and 58d, have a benzylic methylene group, which absorbs as a two-proton singlet near δ3.35. Aside from the different splitting of their methine hydrogen signals, 58a and 58b differ markedly with respect to the absorption of the methyl group. The former exhibits a singlet for the methyl hydrogens, with a chemical shift (δ2.08) indicative of their allylic position. The CH_3 protons of 58b absorb further upfield (δ1.25) as a doublet, the signal being split by the adjacent methine hydrogen. The nmr spectra of indenes 58c and 58d are quite similar, with only subtle differences. The methylene hydrogens adjacent to the cyclopropane ring absorb 17 cycles per second (cps) further downfield in 58c, indicating a slight deshielding effect from the nearby benzene ring.

The best clues to the structures of 58c and 58d came from isomerization studies carried out on the other two products. When 58a was heated in benzene at 200° for 22 hr, the sole product was identical to 58c. A similar thermolysis of 58b yielded only an indene with the same



58a

58c



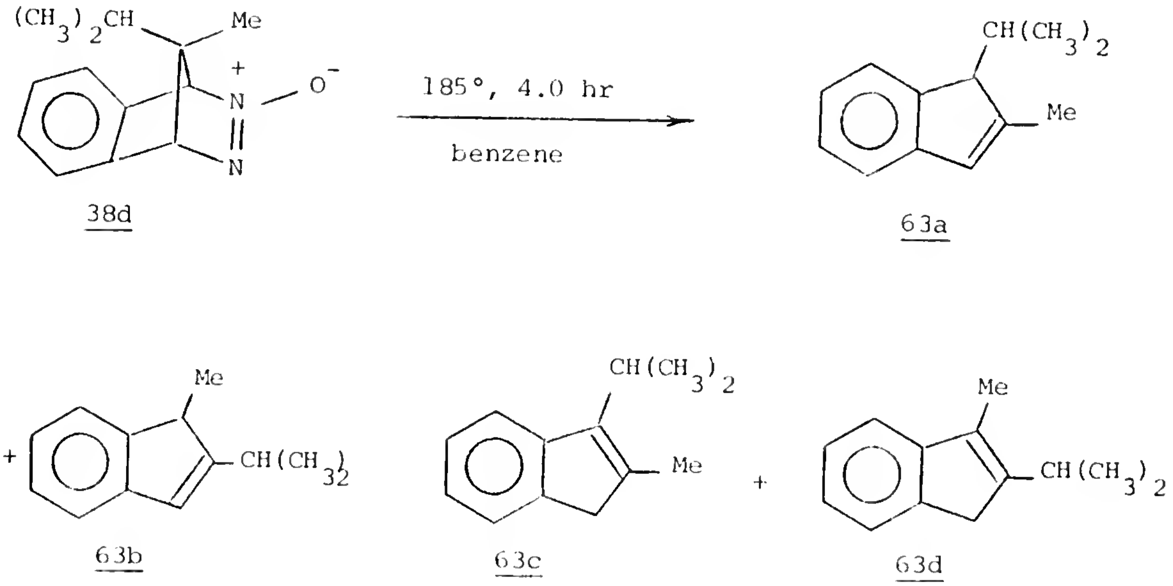
58b

58d

properties as 58d. These results are rationalized as involving the shifting of hydrogens, with no migrations of the substituents. On this basis, 58c is the isomer that has the cyclopropylcarbinyl group at the 3-position.

Azoxy compound 38d, containing an isopropyl and a methyl substituent, was thermolyzed a number of times in benzene. The average reaction was carried out at 185° for 4.0 hr, causing 95% of the starting material to lose nitrous oxide. Based on this extent of reaction, the total product yield was 96% under this set of conditions. The use of either nitrogen (at 1 Atm) or a vacuum (with a degassed solution) in the sealed pyrex tubes had no apparent effect on the experimental results. The product mixture from the average thermolysis contained just four compounds, each with a molecular weight of 172: 1-isopropyl-2-methylindene (63a), 1-methyl-2-isopropylindene (63b), 2-methyl-3-isopropylindene (63c), and 2-isopropyl-3-methylindene (63d).

The nature of the product distribution was similar to those observed for the systems in which R was ethyl (56a-d) or cyclopropylcarbinyl (58a-d).



38d

63a

63b

63c

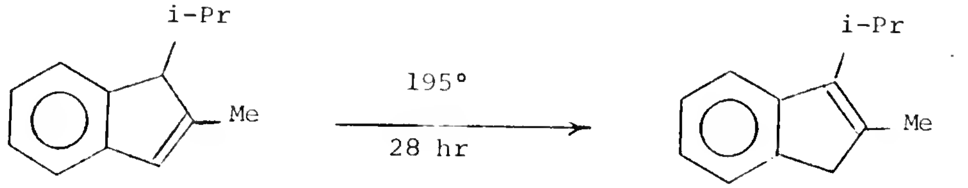
63d

The major product, 63a, was the indene formed solely by the [1,5] shift of the larger alkyl group from the isoindene intermediate (24d). Isomer 63a constituted 81% of the product mixture for an average reaction. The use of milder thermolysis conditions (178° for 3.0 hr) caused less of azoxy 38d to react, and altered the product distribution. The percentages of 63a and 63b in the product mixture were increased relative to those of the more thermodynamically stable indenes 63c and 63d. On the other hand, reactions carried out at or above 190° (for 3-4 hr) not only decomposed all of the azoxy compound, but yielded product mixtures richer in 63c and 63d than that of the average (185°) thermolysis.

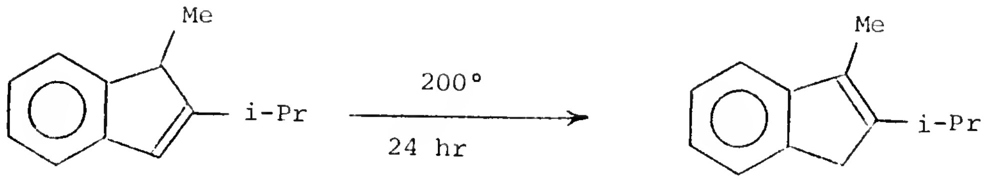
The structures of the 1,2-dialkylindenes, 63a and 63b, were assigned on the basis of their nmr spectra, and both isomers can easily be differentiated from the 2,3-dialkylindenes, 63c and 63d. Since only the former pair of products contain a vinyl hydrogen, only their nmr spectra exhibit a one-proton multiplet around δ6.40. They also show a one-proton signal for the benzylic methine hydrogen at C-1, which absorbs near δ3.25. Lacking these two types of signals, indenes 63c and 63d have instead a broad, three-proton multiplet in the δ2.70-3.50 region, due to the overlapping absorptions of the benzylic methylene group and the isopropyl methine hydrogen. A very distinctive spectral characteristic of product 63a is its upfield pair of tall doublets, at δ0.59 and 1.15. These three-proton signals are caused by the two isopropyl CH_3 groups, which are not equivalent, due to their diastereotopic relationship. On the other hand, all three methyl groups of 63b have similar chemical shifts, and absorb as a nine-proton multiplet around δ1.25. Concerning the nmr spectra of 63c and 63d, the main difference is the chemical shift of the six-proton doublet, for the CH_3 hydrogens of the isopropyl group.

The doublet of 63c is 18 cps further downfield, due to the closer proximity of the aromatic ring to the isopropyl group.

Two isomerization studies helped to assign the structures of the 2,3-dialkylindenes. When indene 63a was heated in benzene for 28 hr at 195°, approximately 70% of it converted to a single product, having nmr and ir spectra identical to those of 63c. Thermolysis of 63b at 200° for 24 hr resulted in roughly a 90% conversion to a product having the same spectral properties as 63d. Since only hydrogen migrations are thought to be occurring in these isomerizations, it follows that the isopropyl group is in the 3-position of 63c, and in the 2-position of indene 63d.



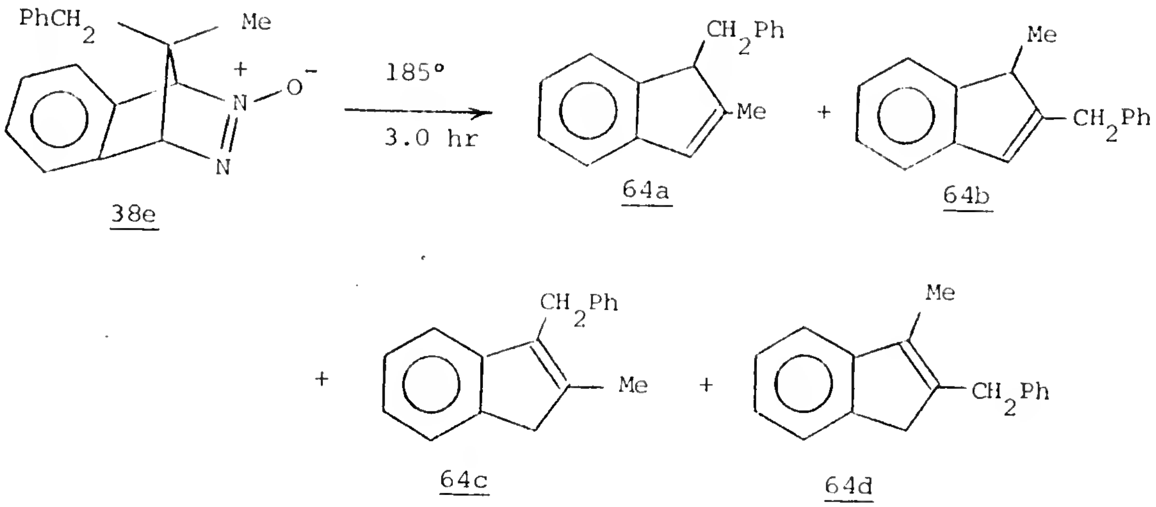
63a 63c



63b 63d

The last system studied was that involving benzyl and methyl substituents. The appropriate azoxy compound, 38e, was thermolyzed several times in benzene, with the average set of conditions being 185° for 3.0 hr. As with the other systems studied, it did not matter whether a vacuum or a nitrogen atmosphere was used in the sealed tubes. In the average reaction, only four isomeric products were observed. They had molecular weights of 220, and the total product yield was 97%. Consistent with the previous studies, the major product had the larger substituent at C-1, as 1-benzyl-2-methylindene (64a). On the average, the major product constituted about 88% of the product mixture. The other three products were believed to be 1-methyl-2-benzylindene (64b), 2-methyl-3-benzylindene (64c), and 2-benzyl-3-methylindene (64d). Approximately 2% of the starting material did not react when heated to 185° for 3 hr.

The effects of using milder or harsher reaction conditions were similar to the results of the other systems studied. Heating azoxy 38e to 175° for 3.2 hr caused only 91% of it to react, and 96% of the product mixture consisted of just one compound, isomer 64a. One of the hydrogen-rearranged products, 64d, was barely noticeable on a gas chromatogram. Thermolysis for 3 hr at the above average temperature of 190° used up over 98% of the starting material, and shifted the product distribution slightly in the other direction, as the amount of 64a in the product mixture fell to 83%.

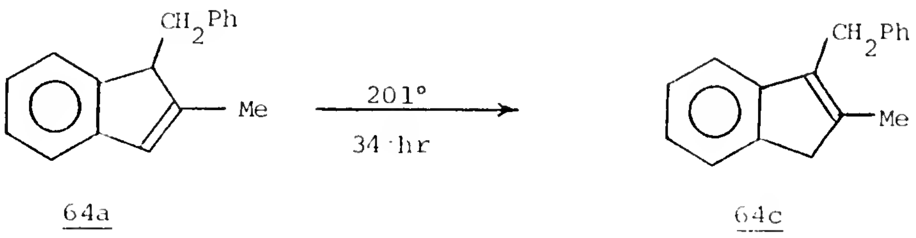


38e 64a 64b 64c 64d

In one experiment, a 50:50 solution of cumene and benzene was used as the thermolysis solvent. Heating at 190° for 4.0 hr resulted in the formation of benzyl, methyl-indenes, and no toluene was found in the product mixture.

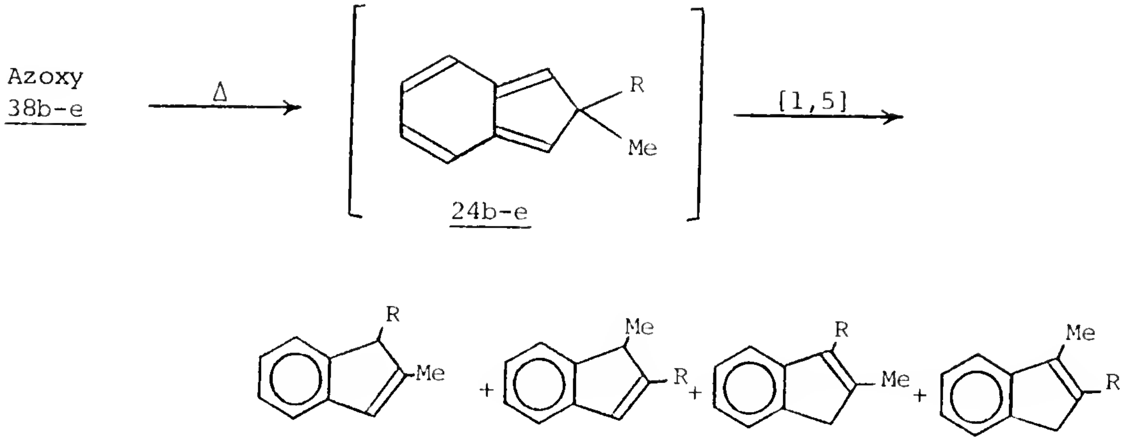
Indenes 64a and 64c were the only products characterized by nmr spectroscopy. Isomers 64b and 64d were very scarce in the product mixtures, and the glpc retention-time differences were relatively small for the four indenes. As a result, the isolation of pure samples of 64b and 64d was an impractical task. The clearest distinction between the nmr spectra of 64a and 64c is a narrow multiplet in the δ6.30-6.57 region for the former isomer, due to its vinyl hydrogen. In contrast, indene 64c has two singlets for its benzylic methylene groups, at δ3.42 and 3.96. The mass spectra (ms) of all four products exhibit a base peak at m/e 91, corresponding to the benzyl substituent of each isomer. The next largest ms peak is at m/e 129, which is the weight of the remaining fragment after benzyl is removed.

More evidence for the structural assignment of 64c came from the isomerization study carried out on purified 64a. Its thermolysis at 201° for 34 hr caused approximately a 70% conversion into a single product, which had nmr and ir spectra identical to those of 64c. Since this set of reaction conditions was only expected to cause hydrogen migrations in 64a, isomer 64c should have the benzyl group at the 3-position.



Relative Migratory Aptitude Determinations

The relative migratory ability of R versus methyl (where R is ethyl, cyclopropylcarbinyl, isopropyl, or benzyl) was determined for [1,5] alkyl migrations in the series of transient isoindenes 24b-e. Ratios were obtained from the quantitative glpc analyses of the product mixtures resulting from the thermolyses of azoxy compounds 38b-e. The a and c indenes of each product mixture are the ones that formed via migration of the R group. Isomers b and d evolved from a [1,5] methyl shift in the isoindene intermediate. Thermolysis results indicate that isomers a and b are the initial products of [1,5] R or methyl rearrangement, respectively. It has been demonstrated that isomer c then formed from a via the shifting of a hydrogen atom; indene d formed from b in the same manner.



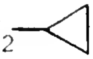
R = Et	:	56a	56b	56c	56d
CH$_2$ 	:	58a	58b	58c	58d
i-Pr	:	63a	63b	63c	63d
CH$_2$Ph	:	64a	64b	64c	64d

For each system, the relative peak areas of the a, b, c, and d indene components were carefully measured. The sum of the relative peak areas of isomers a and c, divided by the sum of the relative peak areas of isomers b and d, constituted the relative migratory aptitude. This value is a direct reflection of the relative rate of [1,5] migration in the isoindene system, for R as compared to methyl.

$$\text{Relative Migratory Aptitude of R:Me} = k_{rel}\left(\frac{R}{Me}\right) = \frac{\underline{a} + \underline{c}}{\underline{b} + \underline{d}}$$

Table 2

Relative Migratory Aptitude of R Versus Methyl*

Azoxy Compound	R	R Migration / Me Migration	Standard Deviation
38b	Et	6.19	0.25
38c	CH_2 	7.85	**
38d	i-Pr	5.27	0.07
38e	CH_2Ph	55.49	4.13

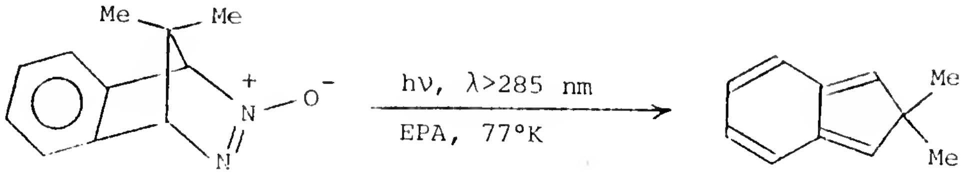
*See Table 8 for more detailed information about individual runs.

**This ratio is based on only one thermolysis reaction.

CHAPTER III
DISCUSSION

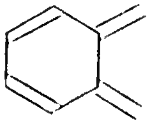
The 2,2-dialkylisoindenes 24a-e, generated during the thermolyses of azoxy compounds 38a-e, were not stable under the reaction conditions. Evidence for their existence as transient intermediates came from bimolecular trapping experiments, which were designed to intercept the isoindenes at 180-190°, before [1,5] alkyl migration could occur. Successful coupling to dimethyl maleate or dimethyl fumurate (good Diels-Alder dienophiles) resulted in high yields of [4+2] cycloaddition products. In each case, the Diels-Alder trapping reaction proceeded in a stereospecific manner, forming just one adduct. The stereospecificity indicates that the 2,2-dialkylisoindenes behaved as simple dienes in this respect, rather than as triplet (diradical) species.

Further evidence for the existence of a dialkylisoindene intermediate was furnished by the isolation and characterization of 2,2-dimethylisoindene (24a), in experiments performed by other researchers. Michl, Horak, and Dewey generated this compound at 77°K, during the irradiation of azoxy 38a, which was dissolved in an ether-pentane-alcohol (EPA) glass matrix.[58,59] The photochemical extrusion of nitrous oxide at 77°K yielded a matrix of 24a that was stable even when melted and allowed to warm to room temperature, as long as no oxygen was present. The pale yellow isoindene exhibited a λ_{max} of 405 nm and a light blue fluorescence (λ_{max} = 467 nm). Similar spectral properties were found for ortho-xylylene (65): λ_{max}(absorption) = 373 nm, and λ_{max}(emission) = 456 nm.[40] The absorption and fluorescence spectra of 24a are also similar to those of the o-quinodimethane derivative 66, which as a planar π-system.[60]

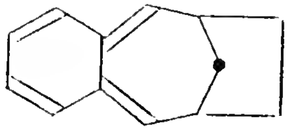


38a

24a

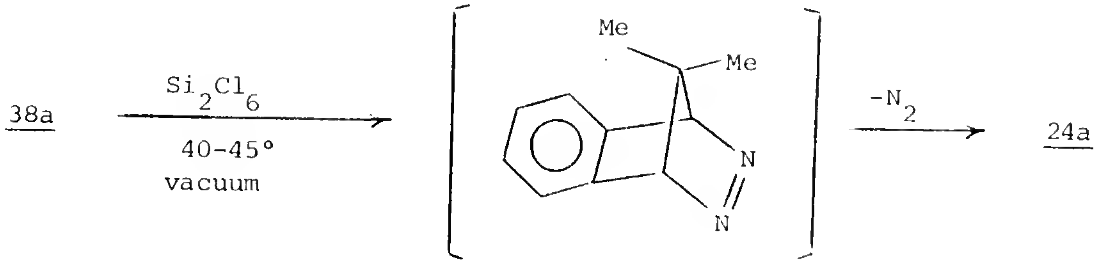


65

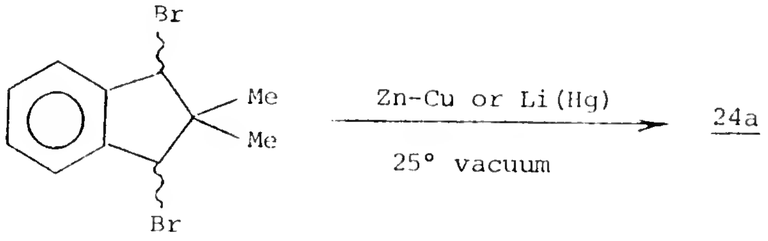


66

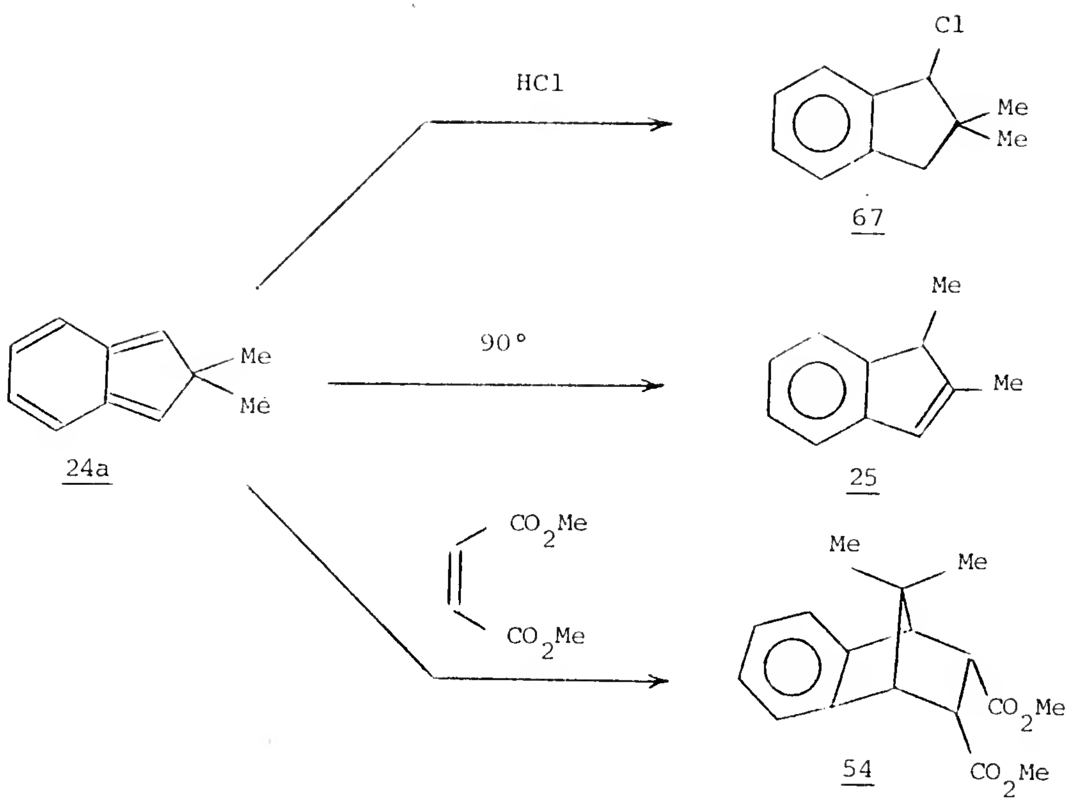
In view of the apparent ability of the gem-dimethyl substituents to stabilize the isoindene toward oligomerization, Dolbier and Matsui attempted to generate 24a at room temperature by an alternative method. Treatment of azoxy 38a with hexachlorodisilane (Si_2Cl_6) at 40-45°, in the absence of oxygen, yielded 2,2-dimethylisoindene as the major product.[58,59] In this reaction, 38a was believed to undergo deoxygenation to a transient benzobicyclic azo compound, followed by a loss of nitrogen to give 24a. (Such an azo compound is consisdered to be unstable at 25°.[40]) These workers also prepared 2,2-dimethylisoindene



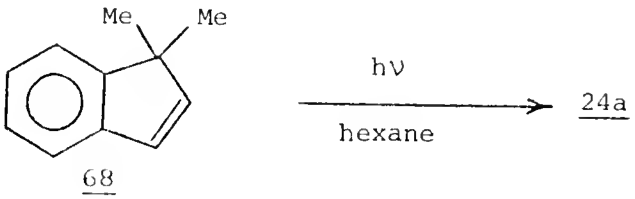
by reacting 1,3-dibromo-2,2-dimethylindane (50a) with zinc-copper couple or lithium amalgam. The dehalogenation of 50a with metals proceeded smoothly at room temperature, and the exclusion of oxygen was essential. Even in quite concentrated solutions, 24a was stable at 25° for many hours. Eventually, the solutions lost their yellow color, with concomitant formation of dimers and/or oligomers. The spectral behavior (uv, nmr, fluorescence, polarized excitation and emission, and magnetic circular dichroism) of 24a was fully in accord with the assigned structure.[59] The nmr spectrum exhibited a six-proton singlet at δ1.16, due to the hydrogens of the two identical methyl groups. There were also vinylic multiplets at δ6.08 (4H) and 6.55 (2H), caused by the absorptions of the protons on the rings. Chemical characterization of 2,2-dimethylisoindene was also preformed. The yellow color of 24a was rapidly discharged when solutions of it were treated with either hydrogen chloride or dimethyl maleate, forming 1-chloro-2,2-dimethylindane (67) or the endo-cis diester adduct 54, respectively. In addition, isoindene 24a was shown to convert thermally to 1,2-dimethylindene (25) at 90°.



50a



At about the same time as the above authors published their results concerning 24a, the isolation of 2,2-dimethylisoindene was also reported by Palensky and Morrison.[61] These researchers photolyzed a dilute hydrocarbon solution of 1,1-dimethylindene (68), which underwent a skeletal rearrangement, yielding a moderately stable solution of isoindene 24a.



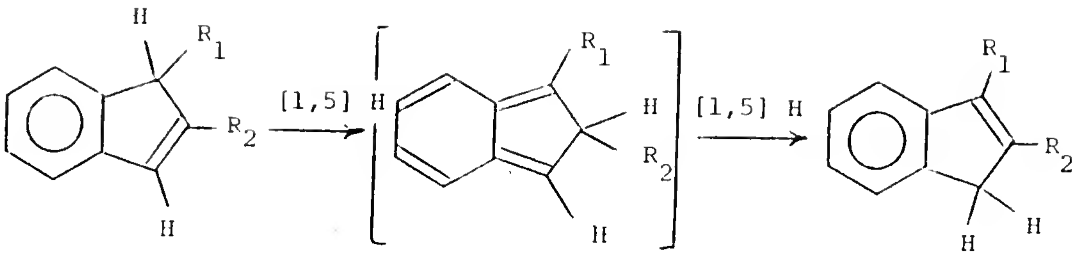
As a result of the interception, isolation, and characterization work performed on 2,2-dimethylisoindene, the existence of this compound as an intermediate during the thermolysis of azoxy 38a has been confirmed.

Not only has it been demonstrated that this benzobicyclic azoxy compound loses nitrous oxide to form 24a, but this isoindene has been shown to thermally rearrange into the primary product of the azoxy thermolysis: 1,2-dimethylindene (25). These results, along with the trapping experiment that intercepted 2-ethyl-2-methylisoindene (57), strongly suggest that dialkylisoindenes 24b-e are also formed as intermediates during the thermolyses of the corresponding azoxy compounds (38b-e).

The existence of a dialkylisoindene intermediate rules out an alternative, concerted mechanism for the transformation of the benzobicyclic azoxy compound into dialkylindene isomers. The loss of nitrous oxide from the azoxy molecule, via a cycloreversion process, occurs in the initial step of the reaction. The resultant isoindene then undergoes the desired [1,5] sigmatropic alkyl rearrangement. The total yield of dialkylindenes (based on the amount of starting material consumed) was essentially constant over the time and temperature ranges employed. This observation indicates that the first mechanistic step, consisting of the nitrous oxide extrusion, is rate-determining.

Due to the transient nature of the dialkylisoindenes in the thermolysis reactions, the rate of their [1,5] alkyl migrations were not able to be measured directly. However, kinetic studies were performed by Dolbier and Matsui on the rearrangement of 2,2-dimethylisoindene (24a) into 1,2-dimethylindene (25). They thermolyzed 24a within the temperature range of 74-105°, and determined the following activation parameters: an activation energy (E_a) of 26.1 ± 1 kcal/mole for the [1,5] methyl migration, with log A = 11.0 ± 0.7. The experimental method used led to a relatively large random error in the rate constants (ca. 15%), but good first order character was observed for the determinations.[62] According to their calculations, using Benson's Group Equivalent Tables,[63] there is about a 20 kcal/mole difference in heats of formation between 24a and 25. This is in excellent agreement with McCullough's approximation from kinetic data.[38] This being the case, and with reported activation parameters of log A = 13.7 and E_a = 45.1 kcal/mole for the [1,5] methyl shift of 1,5,5-trimethylcyclopentadiene (4), one can see that a substantial part of the enthalpic gain incurred by 25 through aromatization is felt in the transition state of the rearrangement. Another indication of the relative ease with which a methyl group migrates in the isoindene system is provided by a comparison of experimental free energies of activation ($\Delta G^{\ddagger}$). The $\Delta G^{\ddagger}$ values, which are insensitive to the balance of log A and E_a, are 29.2 kcal/mole for isoindene 24a and 43.8 kcal/mole for cyclopentadiene 4 at 92.4°, a difference of 14.6 kcal/mole.

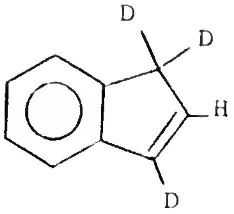
Each of the 1,2-dialkylindene products resulting from the thermolyses of azoxy compounds 38a-e gradually rearranges to the corresponding 2,3-dialkylindene isomer under the reaction conditions. These thermal transformations appear to involve only the shifting of hydrogen, with no alkyl group migration. For the series of dialkylindenes 56 (R = Et), 58 (R = CH_2 ), 63 (R = i-Pr), and 64 (R = CH_2Ph), two successive [1,5] hydrogen shifts constitute the probable mechanism for the conversion of dialkylindene products a and b to products c and d, respectively. The same mechanism applies to the conversion of 1,2-dimethylindene (25) into 2,3-dimethylindene (26). The first [1,5] hydrogen shift (involving the benzylic methine hydrogen at C-1) yields a 1,2-dialkylisoindene intermediate (69), with the migrating hydrogen now located at C-2. This hydrogen then undergoes another [1,5] migration, onto the unsubstituted ring carbon, completing the relocation of the π-bond to a more



a, b or 25 69 c, d, or 26

substituted position. The first step, which breaks up the benzene aromaticity in going to the relatively unstable isoindene 69, would be rate-determining, and should proceed slowly under the usual thermolysis conditions, due to its endothermic nature. This prediction is consistent with the observation that the 1,2-dialkylindenes are moderately stable to rearrangement at 180-190°, during an average thermolysis period of 3-4 hr.

Evidence to support this mechanism comes from various thermal studies on indenes, performed by several research groups. Roth has shown the absolute preference for [1,5] over [1,3] hydrogen (or deuterium) shifts in cyclic systems.[64] He pyrolyzed 1,1,3-trideuteroindene (70) at 220°, which caused the statistical scrambling of hydrogen over all of the non-aromatic ring positions. Roth also pyrolized 1-deuteroindene (71) above 200°, and observed that the distribution of deuterium was not limited to a partition between benzyl positions, but extended statistically over all three of the non-aromatic positions. These results were best explained by invoking the isoindene intermediates 32a and 32b, respectively. Later, when Berson and Aspelin thermolyzed 70 with maleic anhydride in benzene solution, isoindene 32a was trapped as a



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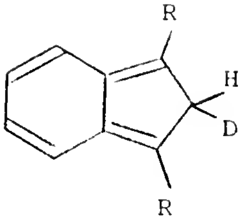
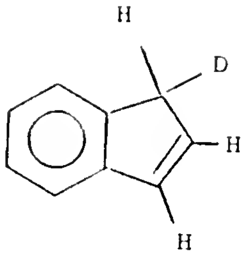


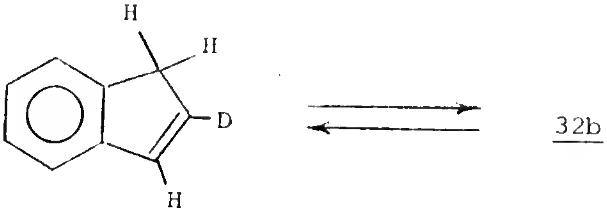
32a: R = D

32b: R = H

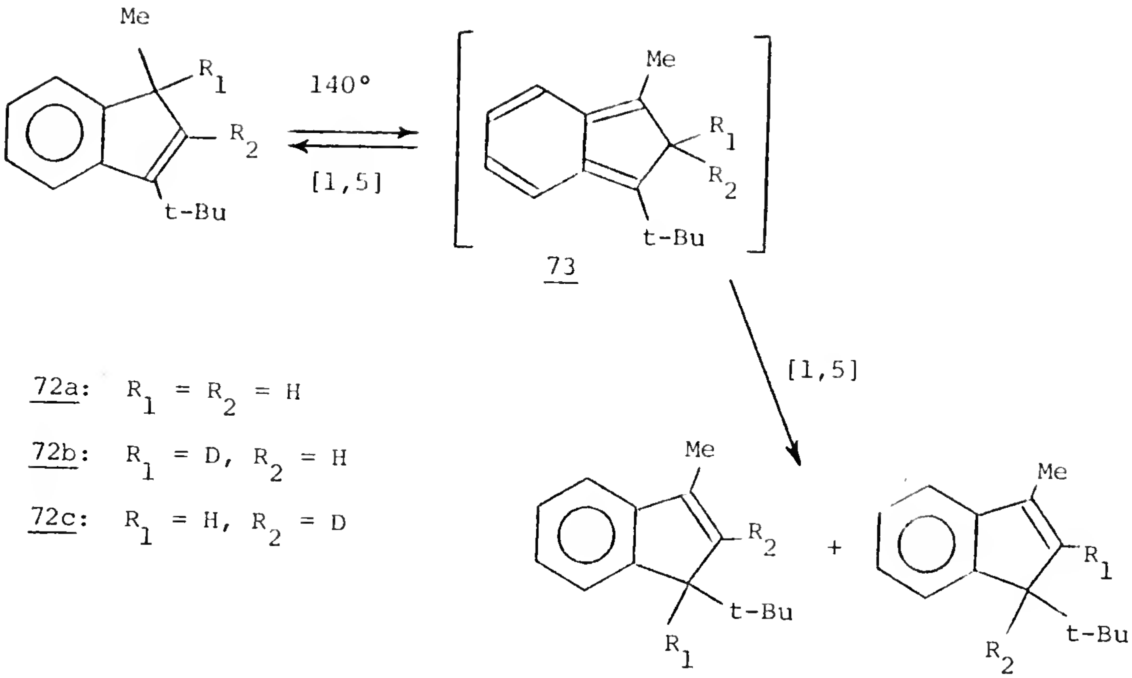


71

[4+2] cycloaddition product.[35] Isaacs similarly intercepted 2-deuteroisoindene (32b), formed as an intermediate during the thermolysis of 2-deuteroindene (in benzene at 210°), via a [1,5] hydrogen shift.[36]



In a related study, Almy and Cram investigated the stereochemistry of hydrogen (and deuterium) migrations in the optically pure 1,3-dialkylindenes 72a-c.[57] These optically active compounds were heated at 140° until partial isomerization occurred, and a 99% racemic product mixture was observed in the case of 72a. This racemization supports the intervention of the isoindene intermediate 73, which is optically inactive when both R_1 and R_2 are hydrogen. In addition, the [1,5] hydrogen (and deuterium) shifts were shown to be suprafacial processes.



73

72a: $R_1 = R_2 = H$

72b: $R_1 = D, R_2 = H$

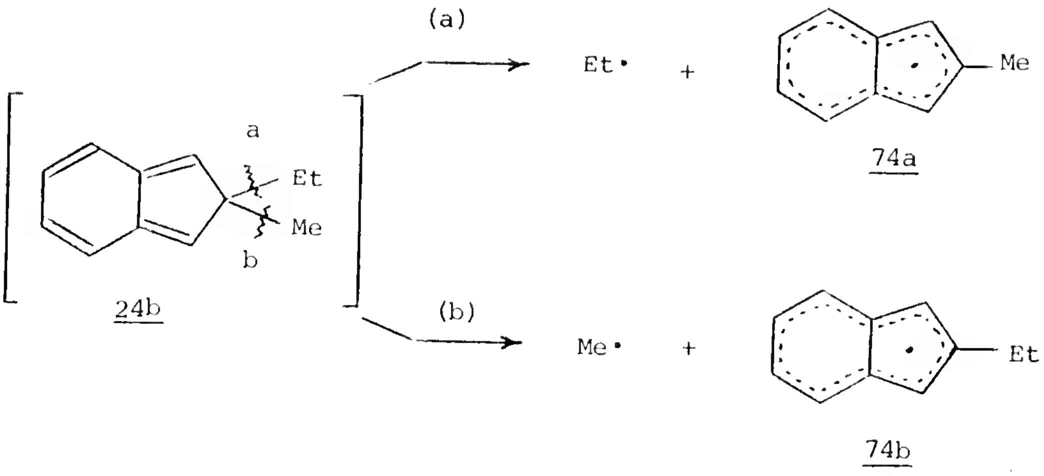
72c: $R_1 = H, R_2 = D$

Two groups of workers have demonstrated that, in the indene system, hydrogen undergoes thermal [1,5] migration much faster than a methyl or an alkyl group. Field, Jones, and Kneen determined relative migratory abilities by studying rates of racemization in a series of substituted indenes (22).[30] Heating at 160-240° caused stereospecific rearrangements. Miller and Boyer studied competitive migrations at 250-300° in indenes 10a-d.[19] The results of both groups were interpreted in terms of a [1,5] shift leading to an isoindene intermediate. All of the kinetic and product analysis data were consistent with concerted, sigmatropic processes.

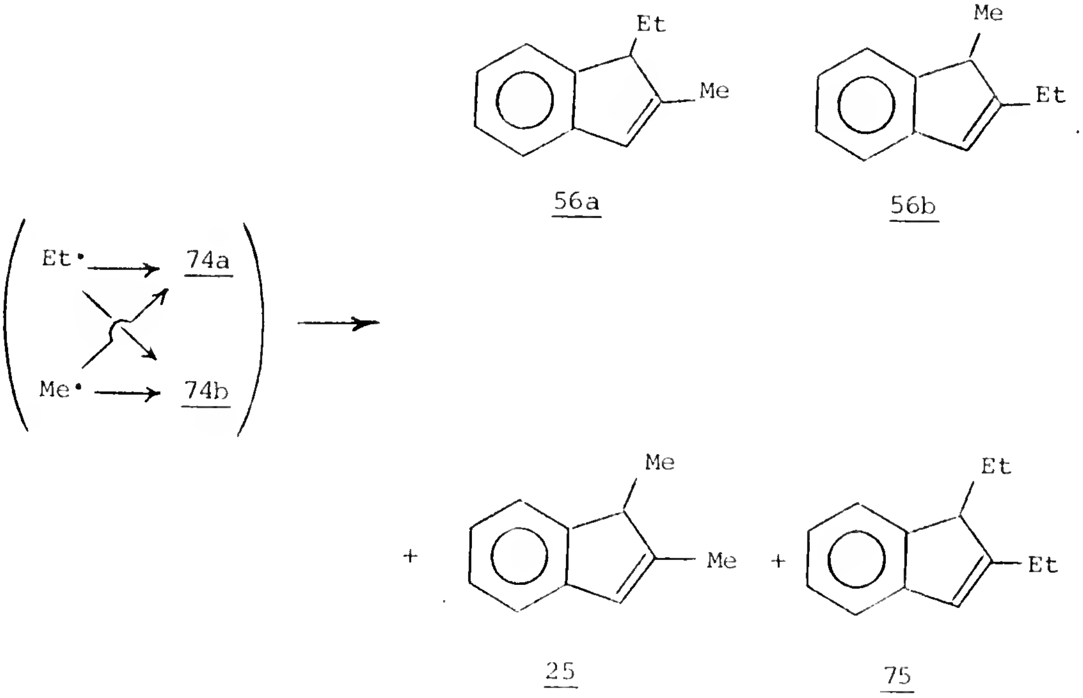
To sum up the results of various experiments dealing with thermal isomerizations in the indene system, [1,5] hydrogen migrations are well-documented reactions in indenes. They are known to result in isoindene intermediates, as well as being a process by which isoindenes can rearrange to indenes. These [1,5] hydrogen shifts are known to occur at 180°; though they proceed slowly at this temperature, corresponding alkyl shifts are not competitive. Finally, [1,5] hydrogen migrations in indenes appear to be sigmatropic processes, due to their concerted, suprafacial nature.

There is good evidence, therefore, that [1,5] sigmatropic hydrogen migrations are solely responsible for the isomerization of each a or b product (a 1,2-dialkylindene in the 56, 58, 63, or 64 series) into the corresponding c or d (2,3-dialkylindene) product, respectively. The alkyl groups remain bonded to the same carbon atom during the transformation. As far as a driving force is concerned, an a to c or b to d rearrangement places the olefinic double bond in a tetrasubstituted position. The product should thus be more thermodynamically stable than the 1,2-dialkylindene starting material.

Concerning the thermal [1,5] alkyl migrations in the 2,2-dialkylisoindenes 24a-e, the results present evidence against a free radical chain mechanism for the rearrangement. To start with, the thermolyses of azoxy compounds 38b-e, in which two different alkyl groups competitively migrate from the isoindene intermediates 24b-e, are inherently crossover experiments. As such, these reactions can indicate whether an alkyl substituent crosses over from one molecule to another. For example, the thermolysis of the ethyl, methyl-azoxy compound (38b) generates the transient 2-ethyl-2-methylisoindene (24b). Either the methyl or the ethyl substituent then migrates in a [1,5] manner, forming a 1,2-dialkylindene as a direct product of rearrangement. If a free radical chain process were involved, initiation would consist of the homolytic cleavage of the σ-bond connecting an alkyl group to the C-2 ring carbon of isoindene 24b. An ethyl or methyl radical would result, along with the 2-methyl- or 2-ethyl-indenyl radical (74a or 74b) as the other fragment, respectively. Each alkyl radical could then attack 74a or 74b, bonding at the C-1 position, to form a 1,2-dialkylindene.

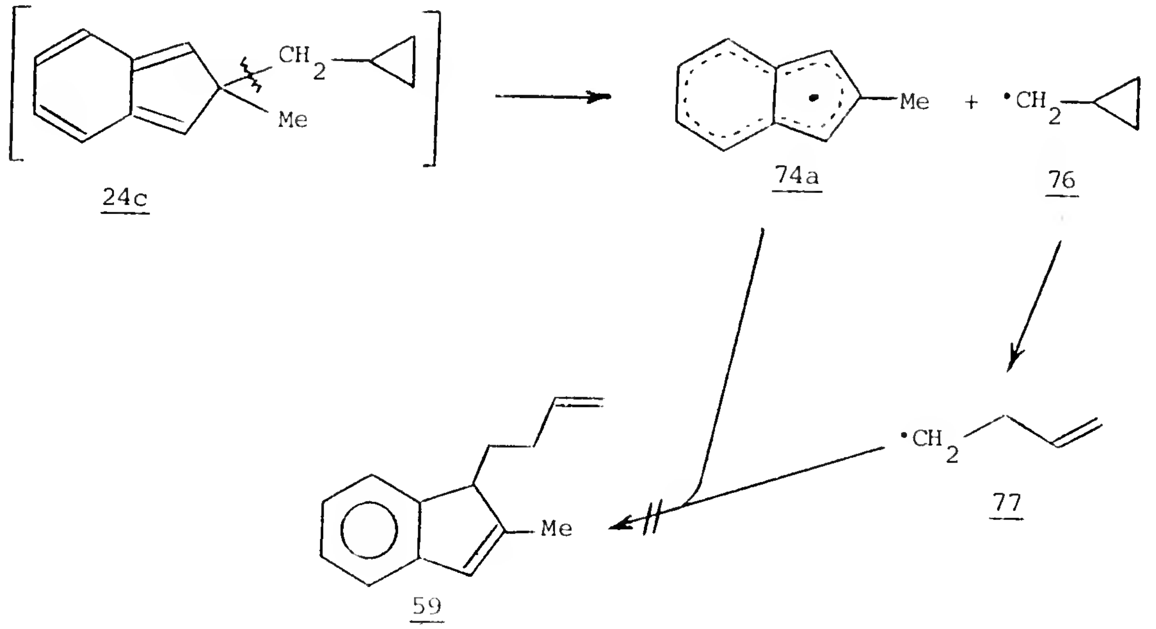


Four compounds would likely form as initial products using this alkyl rearrangement mechanism: 1-ethyl-2-methylindene (56a), 1-methyl-2-ethylindene (56b), 1,2-dimethylindene (25), and 1,2-diethylindene (75).



Indenes 25 and 75 constitute the crossover products, which can only be formed (from isoindene 24b) if free alkyl radicals are generated. However, a careful examination of the product mixture resulting from the thermolysis of azoxy 38b revealed no 75 and less than 0.2% of a component that was potentially the crossover product 25. This rules against the significant intervention of a free radical chain process in the [1,5] alkyl rearrangement. In addition, none of the analogous potential crossover products were observed from the thermolyses of azoxy compounds 38c-e (R = cyclopropylcarbinyl, isopropyl, and benzyl).

A second piece of evidence against the generation of free radicals concerned the fate of the cyclopropylcarbinyl group during its thermal [1,5] migration. A free radical process would involve the homolytic cleavage of the cyclopropylcarbinyl group from the isoindene ring skeleton of 24c. The cyclopropylcarbinyl radical (76) would be expected to isomerize to the allylcarbinyl (3-butenyl) radical (77) under the reaction conditions (180° for 3 hr). When Kochi, Krusic, and Eaton

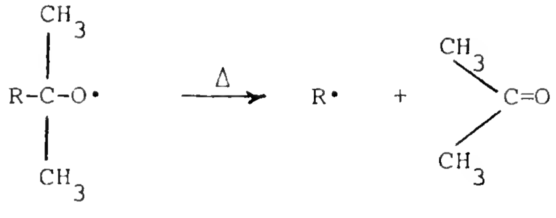


generated 76 via the abstraction of hydrogen from methylcyclopropane, they observed a rapid and irreversible ring-opening isomerization to 77, at temperatures as low as -120°.[65] The absence of any thermolysis products containing a 3-butenyl substituent, such as 59, argues against the formation of cyclopropylcarbinyl radical (76). This result suggests that none of the five migrating groups studied attains full radical character.

In an attempt to intercept any methyl radicals generated from a free radical chain process, cumene was used as a solvent for the dimethyl azoxy compound (38a) during its thermolysis. Cumene is a radical scavenger, which was expected to prevent or significantly reduce the formation of dimethylindene products 25 and 26, if methyl radicals were extruded from 2,2-dimethylisoindene (24a). However, the yield of 25 and 26 was not significantly affected by changing the thermolysis solvent from benzene to cumene. This fact suggests that the [1,5] methyl migration from 24a is either a pericyclic process or one involving a radical cage, instead of being free radical in nature.

In a similar experiment, in which cumene and benzene were used as cosolvents for the thermolysis of benzyl, methyl-azoxy 38e, no toluene was observed in the product mixture. One would expect toluene to be a significant product if benzyl free radicals were formed in the presence of cumene. The lack of toluene formation suggests that benzyl migration is not a free radical process.

Further indication of the pericyclic nature (concerted, with a cyclic transition state) of the alkyl shifts can be derived from the mere 55.5-fold rate enhancement produced when benzyl is the migrating group instead of methyl. While such a rate ratio is certainly indicative of stabilization of the transition state during benzyl migration, the magnitude of this enhancement is not consistent with a fragmentation process being involved, since benzyl-carbon bond-dissociation-energies (BDE's) are generally about 16 kcal/mole less than methyl-carbon BDE's.[63] As a comparison, a benzyl radical was shown to form at a rate 900 times that of a methyl radical, in a reaction where fragmentation is known to occur: in the thermal cleavage of 2-substituted-2-propylalkoxy radicals (78).[66,67] In this case, both bond formation and bond breaking occur in its transition state, whereas the hypothetical cleavage of 2-benzyl-2-methylisoindene (24e) only involves the breaking of a bond.

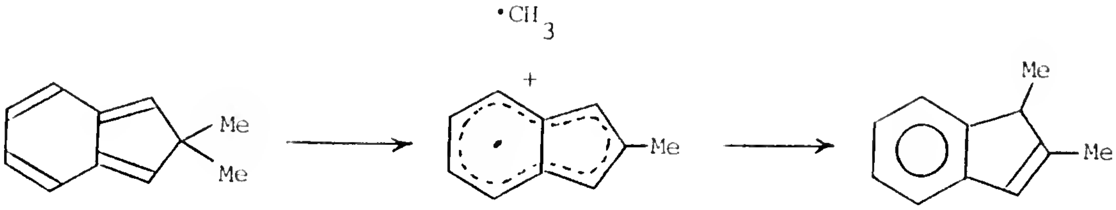


78

Consequently, alkoxy radical cleavage in 78 should be a much less endothermic process than a benzyl cleavage in 24e. One would then expect the migrating benzyl group to have less radical character in the transition state of the former process than in the transition state of the hypothetical isoindene bond scission. The formation of a benzyl radical from 24e would therefore be expected to proceed with a significantly larger rate enhancement (over methyl radical formation) than 900.

By calculating the standard heats of formation (ΔH_f°) for 2,2-dimethylisoindene (24a), 1,2-dimethylindene (25), and for the hypothetical 2-methylindenyl species 74a,[63] one can predict an activation energy of 41 kcal/mole for the dissociation of 24a to 74a, assuming an indenyl radical stabilization energy of about 20 kcal/mole.[62,68,69] The discrepancy between the observed activation energy for rearrangement

(26.1 kcal/mole) and that expected for a dissociative mechanism provides strong evidence that the rearrangement is concerted. In addition, the entropy of activation $(\Delta S^{\ddagger})$ for the rearrangement of 24a into 25 was determined to be -10.6 eu, which is consistent with a concerted process. A



24a 74a 25

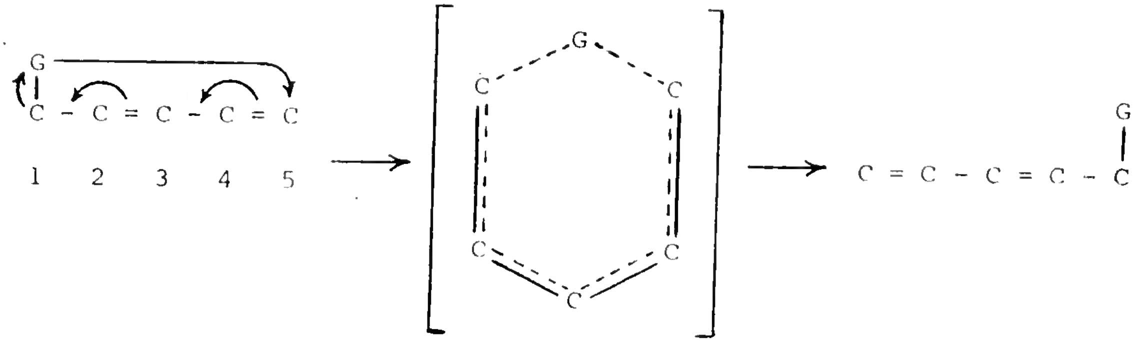
$\Delta H^\circ_f = 41.5$ 82.4 21.9

negative value for the entropy of activation suggests a highly structured or ordered transition state, which would be the case for a pericyclic mechanism.

The relative migratory aptitudes observed in this study (methyl:ethyl: cyclopropylcarbinyl:isopropyl:benzyl = 1:6.2:7.9:5.3:55.5) are consistent with a pericyclic mechanism. The rate enhancement for ethyl, isopropyl, and cyclopropylcarbinyl migration (versus methyl) can be accounted for by considering inductive or hyperconjugative stabilizing effects on such transition states. The electron-donating effect of an alkyl group, though subtle, would help to stabilize the electronic condition at the migrating carbon of of the substituent, during the transition state of the rearrangement. The activation energy for the [1,5] migration of ethyl, isopropyl, or cyclopropylcarbinyl should therefore be slightly lower than for the methyl shift, enough to cause the five- to eight-fold preference for migration of the larger alkyl group on isoindenes 24b-d.

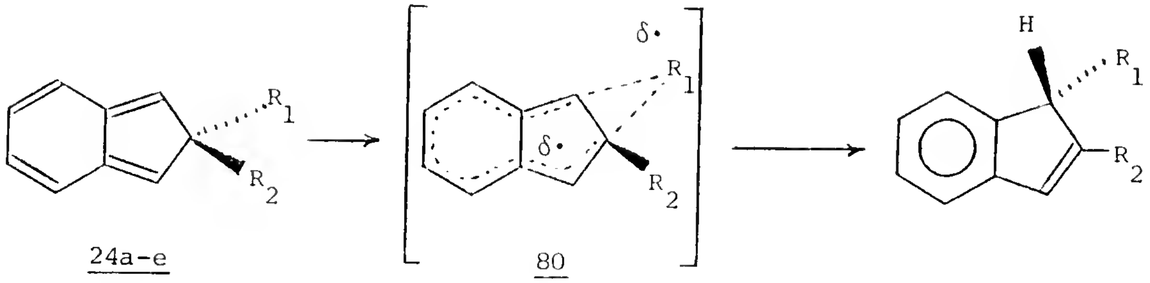
A benzylic carbon atom is the migration site during the [1,5] shift of a benzyl group. In this case, the transition state would be more effectively stabilized by resonance delocalization, compared to the inductive stabilization in simple alkyl groups. Consequently, [1,5] benzyl migration should involve the most stable transition state, and the lowest activation energy, of the sutstituent groups studied in the isoindene system. In this way, benzyl can be predicted to have the largest value of relative migratory aptitude.

As pericyclic processes, the alkyl shifts in this study are categorized as thermal [1,5] sigmatropic reactions. In general, [1,5] sigmatropic rearrangements proceed in a concerted manner through a six-membered cyclic transition state (79), in which the migrating group is partially bonded to both the migration source and migration terminus of the pentadienyl chain. The [1,5] code indicates that bonding in both the reactant and the product is to the same atom of the migrating group, while the migration source and terminus are four carbons apart on the pentadienyl chain. According to the Woodward-Hoffmann Rules, such rearrangements should be suprafacial, with retention of configuration in the migrating group.[1]



79

For the [1,5] sigmatropic alkyl migrations in isoindenes 24a-e, σ-bond breaking in the transition state (80) occurs between C-2 of the isoindene skeleton and its point of attachment on the migrating group (R_1). Simultaneously, a new σ-bond starts to form between the same migrating carbon and C-1 of the indenyl moiety. In terms of an orbital symmetry approach, the transition state for alkyl migration can be envisioned as the interaction between the HOMO (ψ_5) of the 2-alkylindenyl radical and the HOMO (sp^3 orbital) of the migrating group.[28,29,37,57,70] (See Figures 1 and 2.) Since a node exists in the HOMO (ψ_5)



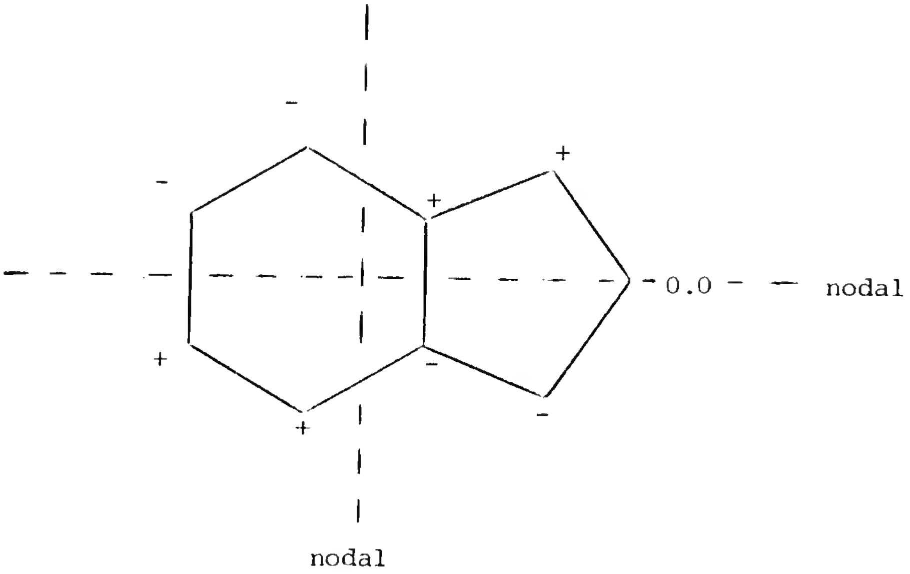
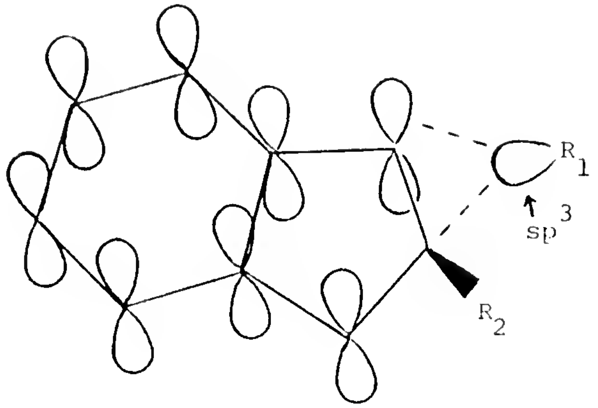


Figure 1: The highest occupied molecular orbital (ψ_5) of indenyl radical



indenyl ψ_5

Figure 2: A molecular orbital model for the transition state of [1,5] alkyl migration in the isoindene system

at the migration source (C-2), with either a plus or a minus lobe serving as the migration terminus, there is no violation of orbital symmetry during the rearrangement.

The alkyl rearrangement mechanism offered thus far appears to be inconsistent with just one result: the slightly higher migratory aptitude of ethyl relative to isopropyl. It should be noted, however, that the relative migratory aptitude values for ethyl, isopropyl, and cyclopropylcarbinyl are fairly close. Due to the uncertainties or deviations associated with these determinations, one cannot be absolutely sure of the ordering of migratory aptitudes among these three substituents. It may not be worthwhile, therefore, to try to account for the small difference in migratory behavior between ethyl and isopropyl.

Concerning the transition states of the [1,5] shifts of ethyl and isopropyl, one would expect the electronic condition at the migrating carbon to be slightly more stabilized in the isopropyl group (since isopropyl contains two CH_3 groups versus one on ethyl). Based on a conventional radical stability argument, one would have predicted a higher migratory aptitude value for isopropyl than for ethyl.

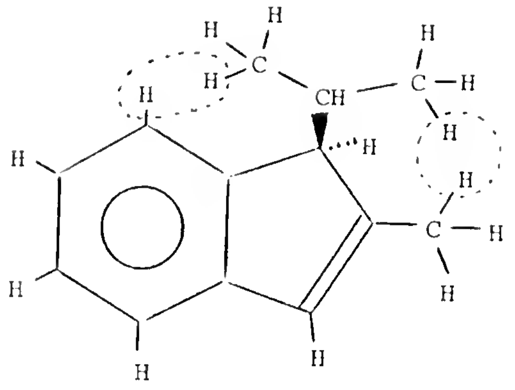
The explanation for this apparent anomaly may not involve the transition state. The rates of [1,5] alkyl migration in the isoindene system can depend on three factors:

(1) the strength (absolute bond dissociation energy) of the bond connecting each alkyl group to the isoindenyl skeleton,

(2) the resonance or inductive stabilizing ability of each alkyl substituent, and

(3) an electronic or steric ground state effect (in the 2,2-dialkylisoindene), or a similar phenomenon in the 1,2-dialkylindene product.

A study of molecular models suggests that steric crowding in the alkyl rearrangement product may be the primary factor controlling the relative migratory rates of isopropyl versus ethyl. When ethyl or isopropyl has migrated to the benzylic carbon (C-1), two steric interactions are encountered: between the migrated group and the methyl substituent remaining on C-2, and between the migrated group and the nearest aromatic hydrogen (at C-7). The migrated isopropyl group can encounter each type of steric hindrance in two conformations, since it contains two CH_3 groups with which to sterically interact. For a migrated ethyl substituent, each type of steric hindrance is only encountered in one conformation. In addition, there is one conformation of an isopropyl group at C-1 in which both steric interactions can occur simultaneously (see Figure 3). Consequently, an isopropyl group appears to face a larger steric barrier toward migration than does an ethyl substituent. This could explain the lower migratory aptitude of isopropyl relative to ethyl, providing that this steric effect more than offsets the transition state advantage of isopropyl migration.



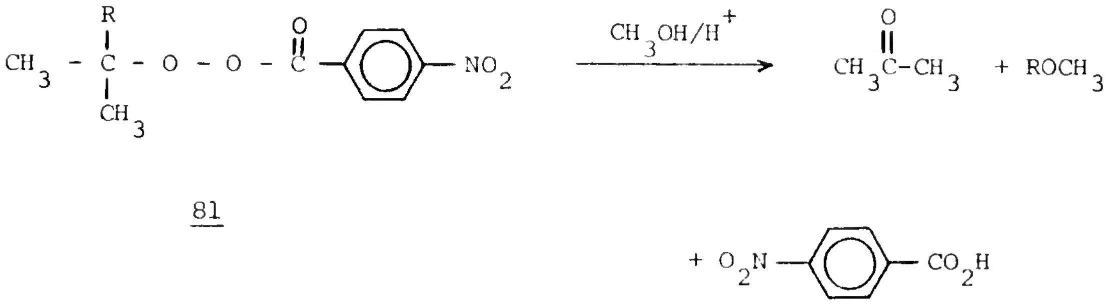
63a

Figure 3: The two principal steric interactions in 1-isopropyl-2-methylindene.

According to Ruchardt, not all phenomena involving radicals can be explained in terms of free radical stabilities. He has proposed that a significant part of the difference in BDE's of methyl-C, ethyl-C, isopropyl-C, and tert-butyl-C bonds may be attributed to ground state effects, and that the inate BDE's of the alkyl-C bonds are very similar.[71] For example, back strain could effectively reduce the apparent dissociation energy of a bond to a bulky substituent.

Ground state effects can often be significant, since for many radical-forming reactions, the transition state possesses much of the character of the ground state. In many cases where radicals are formed by dissociative or abstraction processes, such ground state effects can be invoked to effectively explain the 3°>2°>1°>CH_3 order of reactivity. Similarly, in free radical addition processes, the observed regioselectivity may also be rationalized on the basis of steric effects.[71] Thus, ambiguity exists regarding the actual relative stabilities of various simple alkyl radicals.

The relative migratory aptitudes determined in the study of isoindenes 24a-e may be reflecting the relative stabilities of methyl, ethyl, isopropyl, cyclopropylcarbinyl, and benzyl radicals, even though the suggested pericyclic mechanism attains at most only partial radical character. In similar processes involving pericyclic carbonium ion rearrangements, such as in the peroxyester 81, the migratory aptitudes of methyl, ethyl, isopropyl, tert-butyl, and benzyl were found to reflect their relative carbonium ion stabilities.[67,72]



81

Me : Et: i-Pr : t-Bu : CH_2Ph = 1 : 45 : 2940 : 228,000 : 1630

Again, one must be careful in placing too much significance on small differences in the observed relative rates of [1,5] alkyl shifts in the isoindene system. A comparison of isopropyl migration rate with that of ethyl requires the assumption that the methyl migration rate in each case is identical. This is by no means certain, since steric effects of the group "left behind" on C-2 could give rise to varying rates of methyl shifting. Once techniques are developed for accurate and reproducible measurement of the absolute rates of these rearrangements, more meaningful absolute, rather than relative, rate data will become available. At that time, one should be able to address with less ambiguity the question of the relationship of the migratory aptitude of an alkyl group in a sigmatropic process to its radical stabilizing ability.

CHAPTER IV
EXPERIMENTAL

Boiling points and melting points were uncorrected, the latter taken on a Thomas Hoover capillary melting point apparatus. Infrared spectral data were obtained from either a Perkin-Elmer model 137 or a Beckman model IR-10 spectrophotometer, and all absorption bands are listed in cm^{-1}. Nuclear magnetic resonance spectra were obtained from a Varian model A-60A spectrometer, unless specified as the XL-100 model, utilizing TMS as an internal standard. Mass spectral data were determined using an AEI-MS 30 high-resolution mass spectrometer, which was connected to a DS-30 data system. Elemental analyses were performed by Atlantic Microlab, Inc. (Atlanta, Georgia).

The glpc qualitative analyses were generally carried out on a Varian Aerograph model 90-P gas chromatograph, equipped with the columns listed in the text. The glpc product ratio analyses were performed on a Hewlett-Packard model 5710A gas chromatograph, with a flame ionization detector. A Vidar Autolab 6300 digital integrator was used to determine relative peak areas.

Pyrolyses were done in a silicone oil bath, and a Hallikainen model 1053-A Thermotrol temperature controller was used to maintain a constant temperature.

All reagents which are not referenced were commercially available.

Syntheses Involved in Making the Azoxy Compounds

Sodium enolate of 2-methyl-1,3-indandione (46)

This salt was prepared according to the procedure of Wislicenus and Kotzle.[45] In a 2 l 3-neck flask equipped with a mechanical stirrer, a reflux condenser, a dropping funnel, and a thermometer, were placed 220 g (0.990 mol) of diethyl phthalate. As this reagent was stirred, 42.5 g (1.85 mol) of sodium were added, in small pieces. Then, 89.0 g (0.871 mol) of ethyl propionate were dropped rapidly into the mixture. With vigorous and continual stirring, the reaction mixture was heated to 110°. Powdering of the sodium began at 100-105°, and the reaction became exothermic. The oil bath was then removed in order to prevent the temperature of the reaction mixture from exceeding 120°. As the reaction began to cool, heating was resumed, and the temperature was kept between 110-115° for 3 hr. During this time, a homogenous red suspension developed, which gradually thickened until stirring became difficult. A liter of hot 95% ethanol (EtOH) was then added over a 10 min period, with continuous stirring and heating. Initially, the mixture hardened into lumps, but they gradually disintegrated. The lumps had mostly dissolved after 3 hr of refluxing, leaving some insoluble white particles. The hot reaction mixture was filtered with suction, using a sintered glass filter, and the residue was washed with hot 95% EtOH. The solvent was removed from the red filtrate under vacuum, leaving 175 g of dark red crude product.

2,2-Dimethyl-1,3-indandione (47a)

A solution containing 182 g (<1 mol) of the crude sodium enolate salt (46) in hot EtOH was placed in an autoclave liner. (The volume of ethanol used was the maximum that could be safely heated in the autoclave.) After cooling this solution, 224 g (1.58 mol) of CH_3I were added. The liner was then placed in an Aminco Superpressure reaction vessel, and the contents were heated to 100° for 5 days. After letting the autoclave cool for 24 hr, a brown solution was obtained. The EtOH was removed under vacuum, and the residue was dissolved in a solvent mixture of ether and water. This two-phase mixture was extracted three times with ether, and the combined extracts were then washed with saturated Na_2CO_3 solution until the aqueous fractions no longer became red. The remaining ether solution was washed with water until neutral and dried over $MgSO_4$. Removal of the solvent under vacuum resulted in 137 g of a yellow solid. Recrystallization was done first in EtOH, and then in hexane (followed, if necessary, by another recrystallization in EtOH). This purification yielded 120 g (79%) of a white solid, mp 107° (lit.[45] mp 107-108°). (The overall percent yield is based on the amount of ethyl propionate used to make 46.) For 47a, nmr (CCl_4): δ1.23 (s, 6H), 7.86 (br. s, 4H); ir (neat, KBr): 2910 (m), 1745 (s), 1705 (s), 1595 (m), 1455 (m), 1280 (s), 1195 (m), 877 (m), 798 (m), 723 (s), 687 (m).

2,2-Dimethyl-1,3-indandiol (49a)

In a 3 l 3-neck flask equipped with a mechanical stirrer, a dropping funnel, a Friedrich condenser, and a drying tube were placed 21 g (0.55 mol) of $LiAlH_4$ and 200 ml of anhydrous ether. A solution containing 79 g (0.45 mol) of indandione 47a in 1 liter of anhydrous ether was added dropwise over a 2 hr period. The resultant mixture was refluxed with stirring for 24 hr, after which the excess $LiAlH_4$ was destroyed by the method of Fieser and Fieser.[73] The quenched reaction mixture was filtered, and the remaining white solid was washed well with ether. The solvent was removed under vacuum from the filtrate, and the residue was allowed to dry. The off-white solid product weighed 73 g (91%): mp 145-150°;

nmr ($CDCl_3$): δ0.93-1.27 (m, 6H), 1.73-2.45 (m, 2H), 4.45-5.07 (m, 2H), 7.30-7.70 (m, 4H, includes a tall single peak at 7.47): ir (NaCl): 3360 (s), 2960 (m), 2875 (m), 1460 (m), 1410 (m), 1380 (m), 1325 (w), 1215 (m), 1175 (w), 1100 (m), 1030 (s), 995 (m), 760 (m), 740 (m).

1,3-Dibromo-2,2-dimethylindane (50a)

In a 3 l 3-neck flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser were placed 270 g (0.997 mol) of PBr_3 in 1 liter of $CHCl_3$. A solution of 83 g (0.47 mol) of the crude diol (49a) in 350 ml of $CHCl_3$ was dropped in, followed by 24 hr of refluxing. After cooling to room temperature, 100 ml of water were added with vigorous sitrring, in order to destroy the excess PBr_3. Separation of the $CHCl_3$ layer, followed by removal of the organic solvent under vacuum, resulted in an orange oil. The crude product was distilled using a Vigreux column, yielding 120 g (84%) of a light yellow oil: bp 109-112°/0.5 mm; nmr ($CDCl_3$): δ1.20-1.49 (m, 6H), 5.09-5.30 (m, 2H), 7.14-7.56 (m, 4H); ir (NaCl, neat): 2975 (s), 2940 (m), 1470 (s), 1395 (m), 1375 (m), 1220 (s), 1185 (s), 1155 (m), 890 (s), 865 (m), 840 (m), 765 (s), 700 (s), 655 (m), 637 (m), 605 (m).

Dimethyl 7,7-dimethyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (51a)

Using 20 mesh Zn, 12 g of Zn-Cu couple were freshly prepared according to the method of LeGoff.[51] The 12 g of couple were then placed in a 500 ml 3-neck flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel. In the flask were also placed 30 ml of dimethylformamide (previously dried by standing for one week over 4A molecular sieves). A solution containing 10 g (0.033 mol) of dibromoindane 50a, 9.8 g (0.067 mol) of dimethyl azodicarboxylate,[74] and 30 ml of dry dimethylformamide (DMF) was added dropwise over a

30 min period to the rapidly stirred Zn-Cu couple. The reaction mixture immediately began to turn green, and it became warm. After completing the addition of the reagents, stirring was continued for about 1 hr, until the reaction mixture cooled to room temperature. The Zn-Cu couple was filtered off, using a Celite pad. Ether and water were then added to the filtrate, with a few milliliters of dilute HCl, in order to dissolve the $ZnBr_2$ precipitate. The resultant mixture was separated, and the aqueous layer was extracted three times with ether. The combined extracts were washed with water, and then dried over $MgSO_4$. Solvent removal under vacuum resulted in 8.7 g (91% yield of crude product) of a light yellow glassy solid. Sublimation (at 100° and a pressure of <0.005 mm) gave a white solid: mp 105-106°; nmr ($CDCl_3$): δ0.75 (s, 3H), 1.23 (s, 3H), 3.73 (s, 6H), 4.93 (br. s, 2H), 7.05-7.49 (m, 4H); ir (CCl_4, KBr liquid cell): 2980 (w), 2945 (m), 1755 (s), 1705 (vs), 1435 (s), 1330 (s), 1220 (m), 1135 (m), 1110 (m), 1065 (m), 945 (m), 806 (m), 762 (s), 682 (m); exact mass - calcd. for $C_{15}H_{18}N_2O_4$: 290.1306, found, 290.1290.

Anal. Calcd. for $C_{15}H_{18}N_2O_4$: C, 62.05; H, 6.25; N, 9.65. Found: C, 62.14; H, 6.29; N, 9.63.

7,7-Dimethyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38a)

A solution of 10.0 g (0.0345 mol) of diester 51a in 100 ml of absolute EtOH was placed in a reaction vessel designed to accommodate a vibromixer,[52] a reflux condenser, gas inlet and outlet tubes, a solid addition funnel, and a rubber septum (fitted on a side arm). After placing 10 g (0.18 mol) of KOH in the solid addition funnel, the solution and the reaction vessel were flushed with argon for 1.5 hr. From this point on, a positive argon pressure and the vibromixing were maintained.

The solution was heated to reflux, followed by the rapid addition of the KOH pellets. After 3.5 hr of refluxing, the hydrolysis step was completed (as indicated by TLC, using Al_2O_3, $CHCl_3$, and I_2), and the reaction mixture was cooled to room temperature. A fairly rapid flow of argon was passed through the vessel during the next part of the reaction sequence. Using a syringe, 50 ml of 70% H_2O_2 were gradually added over a 15 hr period. The slow rate of addition prevented the reaction mixture from rising above room temperature, a condition which is important to the success of the reaction. For convenience, it was possible to leave the reaction overnight at room temperature, under an argon atmosphere. The mixture was extracted with 5 portions of CH_2Cl_2. After drying the combined extracts over anhydrous $MgSO_4$, solvent removal on a rotary evaporator resulted in 5.3 g of a yellow oil. The glpc analysis (2.5 ft x 0.25 in column containing 1% SE-30 Chromosorb W, silanized, operating at 140°) indicated that 55% of the crude product was the desired azoxy compound. The other 45% consisted largely of the keto alcohol side product, 53 (R = methyl). The azoxy compound was separated and partially purified by column chromatography, using 300 g of 80/200 mesh Al_2O_3 as the absorbent, and CH_2Cl_2 as the elution solvent. The Al_2O_3 was coated with DuPont 906 luminescent indicator (5% W/W) which, under ultraviolet irradiation, showed the development of three bands during the elution. The relatively small first band contained nothing of interest, but the large second band consisted of 2.37 g of partially pure azoxy compound. Material obtained from the third band weighed 3.25 g, but glpc analysis indicated that only 20% of it was the desired product. Further purification of the azoxy fraction (from band 2) was done by triturating the solid several times in pentane. The resulting white powder weighed 1.7 g (26%): mp 71-73° (with gas evolution); nmr ($CDCl_3$): δ0.85 (s, 3H), 1.43 (s, 3H), 5.04-5.17 (m, 1H), 5.20-5.37 (m, 1H), 7.17-7.67 (m, 4H); ir (KBr): 3040 (m), 2990 (m), 1510 (vs), 1465 (m), 1360 (m), 1275 (m), 1215 (m), 915 (m), 785 (m), 740 (s), 707 (m); mass spectrum m/e (rel intensity) (no parent peak) 158 (1.3, M^+-NO), 144 (47.1, M^+-N_2O), 143 (10.9), 130 (11.6), 129 (100), 128 (49.5), 127 (16.7), 115 (14.0); exact mass (M^+-N_2O) (no parent peak) - calcd for $C_{11}H_{12}$: 144.09380, found: 144.09371.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.18; H, 6.43; N, 14.88. Found: C, 70.10; H, 6.45; N, 14.89.

2-Ethyl-2-methyl-1,3-indandione (47b)

In a 3 l 3-neck flask was placed a solution containing 174 g (<0.95 mol) of impure sodium enolate 46 in 1600 ml of absolute EtOH. The flask was equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser, and 250 g (1.60 mol) of ethyl iodide were placed in the funnel. The ethyl iodide was added with a moderate drop rate to the deep red enolate solution during a 1 hr period. The reaction mixture was then gently refluxed with stirring for 48 hr. When a few drops of the dark solution were shaken in 4 ml of an aqueous ether mixture, most of the color went to the ether layer, which indicated the near completeness of the reaction. Most of the EtOH and unreacted ethyl iodide was removed from the reaction mixture by using a rotary evaporator. The dark red oily residue was dissolved in 450 ml of a solvent mixture (1:1) of ether and water. This two-phase mixture was extracted 4 times with ether, and the combined ether extracts were then washed in a separatory funnel with portions of saturated Na_2CO_3 solution, until the aqueous wash layer, after shaking became orange instead of red. After washing the red ether solution 3 times with water, the organic solution was dried over anhydrous Na_2SO_4. Removal of solvent under vacuum gave a dark red-brown oil. Distillation of this oily product (73-78°/0.1 mm) resulted in a red crystalline solid, which looked damp and impure. Two or more recrystallizations in hexane yielded 33.4 g (20.4%) of a white crystalline solid, mp 46-47.5° (lit.[47] mp 46-47°). (The percent yield is based on the ethyl propionate used to make 46.) For 47b, nmr ($CDCl_3$): δ0.74 (t, 3H), 1.26 (s, 3H), 1.87 (q, 2H), 7.70-8.14 (m, 4H); ir (KBr): 2925 (m), 1745 (s), 1715 (s), 1603 (m), 1458 (m), 1385 (m), 1375 (m), 1335 (m), 1270 (s), 797 (m), 730 (s); mass spectrum m/e (rel intensity) 188 (76.3, M^+), 174 (12.0), 173 (100), 160 (18.1), 159 (13.4), 145 (34.9), 105 (14.4), 104 (43.4), 77 (20.6), 76 (30.3); exact mass--calcd. for $C_{12}H_{12}O_2$: 188.08370, found: 188.08331.

2-Ethyl-2-methyl-1,3-indandiol (49b)

In a 1 l 3-neck flask equipped with a mechanical stirrer, a reflux condenser with a drying tube, and a dropping funnel were placed 100 ml of anhydrous ether and 8 g (0.2 mol) of indandione 47b in 350 ml of anhydrous ether was added from the dropping funnel, with vigorous stirring, over a 2 hr period. The solid particles became sticky during the addition, forming a gray mass or ball in the mixture, as well as coating the walls of the flask. After the completion of the substrate addition, the gray and white solid particles had mostly dispersed, forming a suspension. The reaction mixture was then refluxed gently with stirring for 24 hr. The excess $LiAlH_4$ was destroyed by the method of Fieser and Fieser[73] and the resulting white precipitate was filtered off. After washing the precipitate well with ether, the combined filtrates were dried over

Na_2SO_4. The removal of solvent on the rotary evaporator gave initially a viscous, slightly opaque, colorless oil. The crude product gradually hardened upon standing, and after 1 day, large white crystals had formed in the glassy solid. The weight of crude soild was 27.7 g (96.9%) and this diol was used in the next reaction without purification: mp 68-95°; nmr ($CDCl_3$): 0.57-1.25 (m, 6H), 1.33-1.92 (m, 2H), 2.73 (broad s, 2H), 4.16-4.91 (m, 2H), 7.04-7.71 (m, 4H); ir (solid film NaCl): 3350 (b, s), 2900 (m), 1610 (w), 1585 (w), 1475 (m), 1445 (s), 1410 (m), 1370 (m), 1040 (s), 1020 (s), 995 (m), 756 (s).

1,3-Dibromo-2-ethyl-2-methylindane (50b)

In a 1 l 3-neck flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser were placed 80 g (0.30 mol) of PBr_3 and 350 ml of $CHCl_3$. A solution containing 25.6 g (0.133 mol) of crude diol 49b in 150 ml $CHCl_3$ was slowly added from the dropping funnel to the stirred PBr_3 solution over a 75 min period. The resultant pale yellow solution was refluxed for 24 hours with stirring. A bright orange residue coated the flask walls below the surface of the clear liquid portion of the reaction mixture. After the mixture cooled to room temperature, 40 ml of water were added with rapid stirring. Much heat was evolved, and most of the orange scum was dislodged from the walls of the flask, and floated as droplets within the reaction mixture. The contents were placed in a separatory funnel, followed by portions of water and $CHCl_3$ used to rinse out the reaction vessel. After shaking the mixture well, the orange droplets gathered into the top liquid phase. The $CHCl_3$ solution (lower phase) was separated and dried over $MgSO_4$. Removal of solvent under vacuum resulted in a clear, orange-yellow oil. Distillation (bp 101-104°/0.125 mm) yielded

37.8 g (89.4%) of colorless, clear liquid product: nmr ($CDCl_3$): δ0.64-1.50 (m, 6H), 1.50-2.27 (m, 2H), 5.03-5.36 (m, 2H), 7.07-7.53 (m, 4H); ir (neat, NaCl): 3060 (w), 2950 (s), 2880 (m), 1610 (w), 1460 (s), 1380 (m), 1220 (s), 1200 (s), 770 (s), 703 (s), 660 (m), 600 (w).

Dimethyl-7-ethyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (51b)

The apparatus and procedure used to prepare 51b are the same as those involved in the synthesis of diester adduct 51a. After placing 12 g of freshly prepared Zn-Cu couple and 30 ml of dry DMF in the reaction flask, a solution containing 10.0 g (0.0314 mol) of dibromoindane 50b, 9.17 g (0.0628 mol) of dimethyl azodicarboxylate, and 30 ml of dry DMF was placed in the dropping funnel. The reaction mixture quickly turned an olive green color and generated heat as the solution of reagents was added to the rapidly stirred Zn-Cu couple. After the 30 min addition period, the mixture was stirred another 30 min until it cooled to room temperature. The mixture was suction-filtered through Celite, and two portions of an ether-water mixture were quickly run through the residue. As the washings combined with the filtrate, $ZnBr_2$ precipitated as a white solid, and it was dissolved by the addition of dilute HCl. After three extractions with ether, the combined extracts were washed twice with water, in order to remove the remaining DMF. Drying the ether solution over $MgSO_4$, and removing solvent on the rotary evaporator resulted in 8.5 g (89%) of a pale yellow, viscous oil. This crude product was suitable for use in the next reaction, without needing purification: nmr ($CDCl_3$): δ0.56-1.34 (m, 6H), 1.35-1.88 (m, 2H), 3.67 (s, 6H), 4.97 (broad s, 2H), 7.00-7.48 (m, 4H); ir (neat, NaCl): 2890 (m), 1750 (s), 1710 (s), 1455 (m), 1435 (s), 1330 (s), 1295 (s), 1240 (s), 763 (m); mass spectrum m/e (rel intensity) 304

(7.5, M^+), 289 (4.1), 275 (28.8) 245 (100), 230 (12.3), 229 (49.6), 143 (42.1), 129 (32.3); exact mass--calcd. for $C_{16}H_{20}N_2O_4$: 304.14220, found: 304.14148.

7-Ethyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38b)

The same equipment and an almost identical procedure were used to make this compound as for the synthesis of the dimethyl azoxy compound 38a. After placing 8.5 g (0.15 mol) of KOH pellets in the solid addition funnel, the air in the reaction vessel was replaced with an argon atmosphere. A solution containing 8.5 g (0.028 mol) of diester 51b in 80 ml of absolute EtOH was injected through the rubber septum into the vessel. The vibromixer was then turned on, and a flow of argon was run through the solution and the vessel for 2 hours. With continual vibromixing and a slight argon flow, the solution was heated to reflux, and the KOH was quickly added. The reaction mixture was refluxed for 4.5 hr, resulting in a golden yellow suspension, with some cream-colored precipitate partially coating the vessel walls. A water bath was then placed around the vessel to help keep the reaction mixture at room temperature during the oxidation step. A total of 42 ml of 90% H_2O_2 was slowly added, via syringe (through the septum) to the reaction mixture. The time involved in the actual dropwise addition was 11 hr, though half of the addition was done during one evening, and the rest of the 90% H_2O_2 was added during the next day. When the vibromixer was stopped, the reaction mixture separated into 2 liquid phases: a small tan layer on the bottom, with approximately 100 ml of yellow solution above. The reaction mixture was extracted 4 times with CH_2Cl_2, and the combined yellow extracts were dried over $MgSO_4$. Removing the solvent under vacuum yielded 5.7 g of tan, viscous oil. Initial purification of the crude product was done by column chromatography, using 180 g of 60-200 mesh Al_2O_3, mixed with 6 g of luminescent indicator, as the adsorbent. Elution with CH_2Cl_2 separated the mixture into two broad yellow bands, and the first band consisted mostly of the desired product. The second band, eluted with $CHCl_3$, largely contained a different oxidation product. The solution fractions collected from the solumn were analyzed by glpc using the same column and conditions involved in the analysis of azoxy 38a. The fractions rich in azoxy compound were combined, yielding 2.65 g of partially purified product. This material was then chromatographed through a second column of Al_2O_3, using CH_2Cl_2 as the eluting solvent. Part of the resultant product was placed in a molecular distillation apparatus. By heating the material to 60°, under a pressure of 0.005 mm (the boiling point could not be measured with this apparatus), 0.75 g of distillate was collected. The viscous distillate was initially colorless, but gradually became pale yellow upon standing. The rest of the re-chromatographed product was triturated with several portions of pentane resulting in 0.48 g of pale yellow, viscous oil. Both methods yielded a reasonably pure product, and the total weights of azoxy compound was 1.23 g (22%) based on the molar amount of diester 51b): nmr ($CDCl_3$): δ0.55-1.45 (m, 8H), 4.92-5.18 (m, 1H), 5.19-5.38 (m, 1H), 7.00-7.63 (m, 4H); ir (neat, NaCl): 3040 (w), 2980 (m), 2895 (m), 1510 (s), 1465 (s), 1360 (m), 1220 (m), 925 (m), 780 (m), 735 (s), 708 (m); mass spectrum m/e (rel intensity) (no parent peak) 172 (2.4, M^+-NO), 159 (15.6), 158 (100, M^+-N_2O), 144 (14.8), 143 (80.0), 130 (12.6), 129 (21.4); exact mass (M^+-N_2O)--calcd. for $C_{12}H_{14}$: 158.1095, found: 158.10884.

Anal. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.33; H, 7.00; N, 13.78.

Cyclopropylcarbinyl bromide

A 1 l 3-neck flask was equipped with a mechanical stirrer and a dropping funnel, and was placed in an ice water bath. The reaction flask was charged with 25 g (0.35 mol) of cyclopropylcarbinol, 95g (0.36 mol) of triphenyl phosphine, and 230 ml of DMF. Then, 55 g (0.34 mol) of bromine were added, drop by drop, to the stirred mixture. Upon completion of the reaction, the mixture was filtered. To the filtrate were added 300 ml of pentane and 500 ml of ice water, and the organic layer was separated. After washing the water layer with 100 ml of pentane, the pentane solutions were combined and dried over $MgSO_4$. The pentane was removed under vacuum, and distillation of the residue yielded 22.5 g (48%) of product, bp 108.5-110.5°/760 mm.

2-Cyclopropylcarbinyl-2-methyl-1,3-indandione (47c)

A solution containing 30 g of impure sodium enolate 46 in 150 ml of EtOH was placed in a 500 ml 3-neck flask, which was equipped with a mechanical stirrer, a dropping funnel, a reflux condenser, and a thermometer. After adding 22g (0.16 mol) of cyclopropylcarbinyl bromide (see the preceeding synthetic procedure) to the stirred solution, the reaction mixture was refluxed for 2 days. After removal of the EtOH on a rotary evaporator, the residue was dissolved in a solvent mixture of ether and water. This mixture was extracted 3 times with ether, and the combined extracts were washed 5 times with saturated Na_2CO_3 solution. The extracts were then neutralized by washing with saturated NaCl solution, and dried over anhydrous $MgSO_4$. After removing the solvent under vacuum, the yellow residue was distilled at 106-110°/0.4 mm.

The purified product weighed 7.5 g (22%, based on cyclopropylcarbinyl bromide): nmr ($CDCl_3$): δ0.00-0.50 (m, 5H), 1.27 (s, 3H), 1.80 (d, 2H, J = 6.5 Hz), 7.77-8.12 (m, 4H).

<u>2-Cyclopropylcarbinyl-2-methyl-1,3-indandiol (49c)</u>

In a 1 l 3-neck flask equipped with a mechanical stirrer, a dropping funnel, a reflux condenser, and a drying tube, were placed 4.0 g (0.11 mol) of powdered $LiAlH_4$ and 70 ml of anhydrous ether. A solution containing 7.5 g (0.035 mol) of indandione <u>47a</u> in 230 ml of anhydrous ether was dropped into the reducing agent during a 30 min period. After refluxing the resultant mixture for 12 hr, the excess $LiAlH_4$ was destroyed by adding 40 ml of ethyl acetate dissolved in 40 ml of ether. The white solid material was filtered off and washed well with ether. The combined filtrates were washed twice with water and filtered through anhydrous $MgSO_4$. Solvent removal on a rotary evaporator resulted in 6.0 g (79%) of pale yellow oil. The diol was used without purification in the next step: nmr ($CDCl_3$): δ0.00-0.30 (m, 3H), 0.40-0.74 (m, 2H), 0.76-1.73 (m, 5H, including a tall doublet (3H) at 0.94), J = 2.5 Hz), 1.84-2.80 (m, 2H), 4.35-5.24 (m, 2H), 7.19-7.63 (m, 4H); ir (neat, NaCl): 3360 (s), 3080 (m), 2940 (m), 1645 (w), 1470 (m), 1380 (m), 1265 (m), 1220 (m), 1025 (s), 915 (m), 830 (m), 760 (s), 735 (s).

<u>1,3-Dibromo-2-cyclopropylcarbinyl-2-methylindane (50c)</u>

In a 250 ml 3-neck flask fitted with a mechanical stirrer, a thermometer, a dropping funnel, and a drying tube were placed 5.4 g (0.020 mol) of PBr_3 and 30 ml of dry benzene. To this solution was added 1.0 g (0.013 mol) of dry pyridine over a period of 5 min. The flask was then surrounded by an ice-salt mixture, cooling the contents to -5°C. A solution containing 6.0 g (0.028 mol) of diol <u>49c</u> and 0.6 g (0.008 mol) of dry pyridine in benzene was added slowly from the dropping funnel, with stirring, over a 1 hr period. The temperature was kept at -5° to -3° during this addition, after which the mixture was allowed to stand for 24 hr at room temperature. The contents were transferred to a 500 ml separatory funnel, along with 50 ml of water. After the organic layer was washed with water and dried over $MgSO_4$, the solvent was removed under vacuum, yielding 4.4 g (46%) of the dibromide. NMR ($CDCl_3$): δ0.00-0.27 (m, 3H), 0.33-0.68 (m, 2H), 0.88-1.59 (m, 5H), 5.24-5.58 (m, 2H), 7.10-7.84 (m, 4H).

Dimethyl 7-cyclopropylcarbinyl-7-methyl-5,6-diaza-2,3-benzobicyclo-(2.2.1)hept-2-ene-5,6-dicarboxylate (51c)

In a 500 ml 3-neck flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser were placed 30 ml of dry DMF and 14 g of freshly prepared Zn-Cu couple.[51] A solution containing 4.4 g (0.013 mol) of dibromoindane 50c, 4.0 g (0.027 mol) of dimethyl azodicarboxylate,[74] and 15 ml of dry DMF was added dropwise to the rapidly sitrred Zn-Cu couple. After the addition was completed, the warm reaction mixture was stirred until it cooled to room temperature. The mixture was filtered through a Celite pad and the residue was washed with water and ether. After collecting the wash solutions in the filtrate, enough dilute HCl was added to dissolve the $ZnBr_2$ precipitate. The liquid layers were separated, and the aqueous layer was extracted three times with ether. The combined ether layers were neutralized and then dried over $MgSO_4$. Solvent removal under vacuum resulted in 3.7 g (86%) of a clear, glassy solid: nmr ($CDCl_3$): δ0.11-0.68 (m, 4H), 0.73-1.00 (m, 3H), 1.33 (s, 3H), 3.75 (s, 6H), 5.01-5.22 (m, 2H), 7.13-7.51 (m, 4H); ir: 2900 (m), 2810 (m), 1740 (s), 1710 (s), 1580 (m), 1425 (s).

7-Cyclopropylcarbinyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38c)

A solution containing 3.7 g (0.011 mol) of diester 51c in 60 ml of absolute EtOH was placed in the same reaction vessel that was used in the synthesis of 38a, fitted with the same accessories. The system was flushed with argon for 2 hr, and then the solution was heated to reflux. With the vibromixer operating, 5.0 g (0.089 mol) of KOH pellets were quickly added from the solid addition funnel. After 2 hr of refluxing, the reaction mixture was cooled to room temperature. The flow of argon through the reaction mixture and the vessel was continued through the next step, and the vessel was kept in a water bath. A total of 25 ml of 70% H_2O_2 were slowly added to the reaction mixture over a period of 8 hr, as the mixture was vibromixed. The H_2O_2 addition was done in a manner similar to that used in the synthesis of 38a. The reaction mixture was poured into a separatory funnel and washed with water. The mixture was then extracted with CH_2Cl_2, the layers were separated. After extracting the aqueous layer with 4 more portions of CH_2Cl_2, the combined organic extracts were filtered through $MgSO_4$. Solvent was evaporated under vacuum, leaving a yellow oil. Purification of this crude product was done in a similar manner as the purification of 38a. The yellow oil was chromatographed through 100 g of 80/200 mesh Al_2O_3 containing a luminescent indicator. The first band (containing the product plus an impurity) was eluted with a 1:1 solution of CH_2Cl_2 and EtOH, and the last band was left on the column.

The azoxy solution was evaporated under vacuum, and the yellow residue was triturated six times with pentane, yielding a solid. The azoxy compound, still slightly impure, was then chromatographed twice through columns of alumina, using benzene as the eluting solvent. The purified, creamy-white powder weighed 0.72 g (29%): mp 81-85° (with gas evolution); nmr ($CDCl_3$): δ-0.11 to -0.35 (10.11-10.35τ, m, 1H), 0.10-1.33 (complex, overlapping multiplets, 6H), 1.37-1.84 (m, 3H, including a tall singlet at δ1.49), 5.08-5.49 (m, 2H), 7.07-7.68 (m, 4H); ir (NaCl, solid film): 3090 (m), 3015 (m), 2950 (m), 1188 (m), 1163 (m), 1024 (m), 980 (m), 915 (m), 830 (m), 788 (m), 775 (m), 740 (s), 710 (m); mass spectrum m/e (rel intensity) (no parent peak) 198 (2.1, M^+-NO), 184 (38.0, M^+-N_2O), 169 (18.7), 143 (82.6), 142 (31.7), 130 (20.0), 129 (66.1), 128 (71.5), 115 (30.4), 77 (10.0), 55 (100); exact mass--calcd. for $C_{14}H_{16}$ (M^+-N_2O): 184.12510, found: 184.12575.

Anal. Calcd. for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.61; H, 7.08; N, 12.25.

2-Methyl-1,3-indandione (48)

In a 2 l separatory funnel were placed 180 g of crude sodium enolate 46 in 1.1 l of water. Most of the salt dissolved, and an opaque, dark red suspension resulted. This mixture was extracted four times with ether, in order to remove unreacted diethyl phthalate and other organic impurities. The ether extracts were discarded, and the aqueous mixture was placed in a 2 l Erlenmeyer flask equipped with a magnetic stirrer. The stirred enolate suspension was acidified with 6N HCl until the pH of the aqueous phase decreased to 2 (approximately 250 ml of acid were required). A dark red oil separated to the bottom as the mixture was acidified. The mixture was extracted four times with ether, giving about 1 l of combined extracts. The red ether extracts were washed with aqueous NaCl solution, in order to remove traces of acid. As the extracts were dried over anhydrous $MgSO_4$, some orange powdery precipitate formed. After filtering off the precipitate and the drying agent, the solvent was removed on the rotary evaporator. The residue was initially a clear, dark red oil, but some crystals gradually formed on the bottom (the entire residue may solidify if allowed to sit for a day or more). When the mixture was transferred to a distillation flask, all of the material solidified into an impure crystalline mass. As distillation was performed (98-115°/0.125 mm), orange-yellow crystals formed in the condenser as well as the receiving flask. A heat gun was used to melt the solid distillate, so that the condenser would not be clogged. The crystalline material was recrystallized twice, using a 2:1 ethanol-water solution as the solvent. Creamy-white granular crystals resulted, weighing 28.8 g (20.7% based on 0.871 moles of ethyl propionate used in the synthesis of 46): mp 83-84.5° (lit.[47] mp 86-87°); nmr ($CDCl_3$): δ1.40 (d, 3H), 3.07 (q, 1H), 7.70-8.20 (m, 4H); ir (neat, NaCl): 2920 (m), 1775 (m), 1745 (s), 1720 (s), 1600 (m), 1468 (m), 1453 (m), 1370 (m), 1345 (m), 1283 (m), 1235 (m), 743 (m).

2-Isopropyl-2-methyl-1,3-indandione (47d)

In a 125 ml Erlenmeyer flask was made a fresh solution of NaOEt in EtOH, by dissolving 2.3 g (0.10 mol) of Na in 100 ml of absolute EtOH. This NaOEt solution was added to a solution of 12.0 g (0.075 mol) of indandione 48 in 100 ml EtOH, contained in another flask. A deep red solution of the enolate anion of 48 formed upon swirling. After flushing an 800 ml pyrex tube with N_2, the enolate solution was poured into the tube, along with 40.0 g (0.235 mol) of isopropyl iodide. An additional 50 ml of EtOH were used to wash down the inner surfaces of the tube, and the tube was then sealed under N_2. The reaction mixture was thermolyzed at 150° for 10 hr, using a tube furnace. A clear yellow-orange solution resulted, and this was poured into 750 ml of water in a 2 l separatory funnel. After shaking the mixture, part of the organic material dissolved, and the rest formed a dark orange top layer. Three ether extractions were done, using 250 ml portions. The combined ether extracts, a yellow solution, was shaken 4 times with aqueous Na_2CO_3 solution, in order to remove unreacted substrate. The first wash became a semi-solid red sludge, and extra water was added to the mixture, so that the aqueous layer could be drained out of the funnel. Shaking with the fourth basic wash only resulted in a pale orange aqueous solution. The ether solution was then washed with 2 portions of aqueous NaCl solution, in order to remove the base. After drying the pale yellow ether solution over $MgSO_4$, solvent was removed under vacuum to give 8.2 g of clear brown oil. The crude product was distilled with a Vigreux column, collecting one fraction of clear, yellow-orange liquid. A yield of 6.7 g (44%) was obtained: the bp ranged from 73°/0.06 mm to 84°/0.18 mm (lit.[48] bp 80°/0.05 mm, or lit.[47] bp 93-97°/0.1 mm); nmr ($CDCl_3$): δ0.94 (d, 6H), 1.28 (s, 3H), 1.84-2.56 (m, 1H), 7.72-8.12 (m, 4H); ir (neat, NaCl): 2975 (m), 2945 (m), 2885 (m), 1745 (s), 1710 (s), 1600 (m), 1465 (m), 1390 (m), 1375 (m), 1335 (m), 1270 (s), 1160 (m), 988 (m), 785 (m), 730 (m); mass spectrum *m/e* (rel intensity) 202 (19.9, M^+), 188 (13.5), 187 (100), 160 (30.6), 159 (8.2), 131 (15.8), 104 (24.9), 77 (12.7), 76 (15.0), 43 (14.3); exact mass--calcd. for $C_{13}H_{14}O_2$: 202.09930; found: 202.09959.

2-Isopropyl-2-methyl-1,3-indandiol (49d)

The apparatus was the same as that used in the preparation of diol 47b, and it was first flushed out with N_2. After placing 7.6 g (0.20 mol) of powdered $LiAlH_4$ and 100 ml of anhydrous ether in the reaction flask, a solution containing 17.3 g (0.0856 mol) of indandione 47d in 250 ml of anhydrous ether was placed in the dropping funnel. The substrate solution was slowly added to the stirred reducing agent over a 2 hr period, and solid gray and white particles developed in the suspension. After refluxing the reaction mixture for 24 hr with stirring, the Fieser[73] method was used to get rid of the remaining $LiAlH_4$. The white-orange, gummy precipitate that formed was filtered off, and washed with two portions of ether. The combined filtrates were dried over Na_2SO_4, and removed of solvent on the rotary evaporator resulted in 17.4 g (98.9%) of a white, sticky crystalline solid. This crude diol was used in the next reaction without purification. After drying in a vacuum dessicator, a flaky white solid resulted: mp 95-109°; nmr ($CDCl_3$): δ0.59 (d, 3H), 0.86-1.30 (m, 6H), 1.74-2.69 (m, 3H), 4.23-4.98 (m, 2H), 7.06-7.45 (m, 4H); ir (NaCl): 3330 (b, s), 2900 (m), 1640 (w), 1470 (m), 1385 (m), 1190 (m), 1035 (s), 1010 (s), 755 (s).

1,3-Dibromo-2-isopropyl-2-methylindane (50d)

In a 250 ml 3-neck flask equipped with methanical stirrer, a dropping funnel, a reflux condenser, and a drying tube were placed 38 g (0.14 mol) of PBr_3 and 130 ml of $CHCl_3$. A solution of 14.1 g (0.0684 mol) of diol 49d in 65 ml of $CHCl_3$ was added from the dropping funnel to the stirred PBr_3 solution over a 75 min period. The dropping funnel had to be heated during the addition (using a heat gun), since the diol began precipitating out of solution. The reaction mixture was refluxed for 24 hr with gentle stirring, and a bright orange coating developed on the vessel walls. After the mixture cooled to room temperature, 20 ml of water were quickly dropped in with vigorous stirring. A considerable amount of heat was evolved, and the orange coating loosened from the walls, forming orange droplets in suspension. In a separatory funnel the quenched reaction mixture plus another 20 ml of water were shaken. When the orange globules rose to the top, the clear organic solution below was collected. The yellow-tinted $CHCl_3$ solution of product was dried with $MgSO_4$, and the solvent was removed under vacuum. A light yellow oil was obtained, weighing 21.5 g (94.7%). The crude product is adequately pure for use in the next reaction. Purification was accomplished by simple distillation, resulting in a clear, slightly yellow and slightly viscous distillate: bp 94-96°/0.045 mm; nmr ($CDCl_3$): δ0.87-1.45 (m, 9H), 2.52 (heptet, 1H), 5.05-5.49 (m, 2H), 7.06-7.58 (m, 4H); ir ($CHCl_3$, KBr cells): 3075 (w), 2965 (s), 2880 (m), 1650 (w), 1605 (w), 1465 (s), 1395 (m), 1375 (m), 1200 (s), 840 (m), 620 (m), 600 (m), 570 (m); mass spectrum <u>m/e</u> (rel intensity) 332 (<0.1, M^+), 253 (5.0, $M^+-{}^{79}Br$), 251 (5.1, $M^+-{}^{81}Br$), 172 (48.9), 157 (90.2), 142 (22.6), 129 (100), 115 (32.4), 82 (19.7), 81 (6.9), 80 (20.2), 79 (7.6), 43 (20.5); exact mass--calcd. for $C_{13}H_{16}{}^{79}Br$: 251.04340; found: 251.04344.

<u>Dimethyl-7-isopropyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (51d)</u>

A batch of Zn-Cu couple was freshly prepared by the method of LeGoff,[51] using 20 mesh zinc. A 250 ml 3-neck flask, equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser, was flushed for 1 hr with N_2. After placing 5.7 g of the Zn-Cu couple and 20 ml of dry DMF in the flask, a solution containing 5.1 g (0.015 mol) of dibromoindane <u>50d</u>, 4.5 g (0.031 mol) of dimethyl azodicarboxylate,[74] and 20 ml of dry DMF was placed in the dropping funnel. The reaction was carried out in the same way that diester <u>51b</u> was prepared, and the same method was used to isolate the product. The observations noted during the reaction and work-up were very similar to those in the synthesis of 51b. The three ether extractions gave 125 ml of a yellow-green solution. The combined extracts were washed twice with aqueous NaCl solution, resulting in a pale yellow organic solution. After removing solvent on the rotary evaporator, a clear, pale yellow, glassy residue was obtained. It was a very viscous semisolid, and weighed 4.5 g (94%). This crude product was used without purification in the next reaction: nmr ($CDCl_3$): δ0.52-1.37 (m, 9H), 1.67-2.27 (m, 1H), 3.70 (d, 6H, in which one peak is much taller than the other), 4.89-5.27 (m, 2H), 7.05-7.58 (m, 4H); ir (neat, NaCl): 2970 (m), 2880 (w), 1760 (s), 1710 (s), 1445 (m), 1335 (b, m), 1230 (s), 765 (m); mass spectrum m/e (rel intensity) 318 (7.9, M^+), 275 (22.9), 259 (29.6), 202 (20.8), 189 (100), 175 (37.3), 171 (66.1), 157 (52.0), 145 (45.6), 143 (38.1), 131 (31.5), 130 (35.7), 129 (58.5), 128 (35.0), 59 (41.9), 44 (32.7), 43 (37.3); exact mass--calcd. for $C_{17}H_{22}N_2O_4$: 318.15790, found: 318.15805.

7-Isopropyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38d)

The apparatus used in this synthesis was the same as that used in the preparation of azoxy compound 38a. The first step in the reaction sequence, the basic hydrolysis--decarboxylation, involved the same operations as those used in the corresponding step for the synthesis of 38b. As a solution of 4.0 g (0.013 mol) of diester adduct 51d in 75 ml of absolute EtOH was refluxed in an argon atmosphere, 3.5 g (0.062 mol) of KOH pellets were quickly added. The vibromixed solution immediately darkened to a tan color. The 4 hr of refluxing resulted in a dark tan mixture, with some cream-colored precipitate coating parts of the vessel walls. For the oxidation step of the synthesis, a water bath was placed around the vessel, and the flow rate of argon through the reaction mixture and the vessel was tripled. With continual vibromixing, a total of 14.5 ml of 90% H_2O_2 were slowly added to the reaction mixture, introduced through the rubber septum by a syringe. During the early stages of the H_2O_2 addition, the mixture became bright yellow, and contained more solid particles in suspension. The addition was done during three 4-hr intervals, spread over a 24 hr period. (Though the H_2O_2 can be continually added over a 12 hr period without interruption, the schedule used was more convenient.) The resultant mixture consisted of a clear yellow solution over a small, non-miscible liquid layer. Some water was added to the reaction mixture as it was placed in a separatory funnel. Four extractions were done with the CH_2Cl_2, and 250 ml of a dull yellow organic solution were obtained. Some NaCl had to be added during the extractions in order to hasten the separation of the layers. After drying the combined extracts over $MgSO_4$, solvent was removed on the rotary evaporator, resulting in 3.2 g of a viscous, dark tan oil. The crude product was chromatographed on a column containing 110 g of 80-200 mesh Al_2O_3 (mixed with 3 g of luminescent indicator), and CH_2Cl_2 was the first eluting solvent. The azoxy compound came off the column not only with the first yellow band material, but also in the colorless fraction immediately following the first band. The presence of the azoxy compound in a given fraction of eluent was quickly determined by glpc analysis, using a 2.5 ft x 0.25 in column containing 1% SE-30 on chromosorb W (silanized), operating at 127°. The second yellow band material was eluted with $CHCl_3$, and was found to contain hydroxy and carbonyl functional groups. The residues from the column fractions were also analyzed for the presence of the azoxy compound by infrared. A strong absorption at about 1510 cm^{-1} is typical of the azoxy group. The partially purified azoxy residues gradually solidified or formed semisolids. Several triturations with n-pentane resulted in a white powder, mp 108-110° (dec). The pure product weighed 0.67 g (24%): nmr ($CDCl_3$): δ0.75 (t, 6H {on the Varian model XL-100 nmr, this signal appears as two doublets}), 0.98-1.64 (m, 4H {includes a large single peak at 1.24}), 5.08 (d, 1H), 5.20-5.47 (m, 1H), 7.05-7.67 (m, 4H); ir (KBr pellet): 3040 (w), 2975 (m), 2890 (w), 1515 (s), 1460 (s), 1365 (w), 775 (m), 730 (s), 710 (m); mass spectrum m/e (rel intensity)(no parent peak) 186 (0.2, M^+-NO), 172 (51.5, M^+-N_2O), 158 (14.3), 157 (100), 142 (27.2), 141 (18.8), 130 (54.7), 129 (85.1), 128 (47.5), 127 (19.3), 115 (37.4), 43 (19.5); exact mass--calcd. for $C_{13}H_{16}$ (M^+-N_2O): 172.12510, found: 172.12519.

Anal. Calcd. for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found, C, 72.21; H, 7.47; N, 13.00.

2-Benzyl-2-methyl-1,3-indandione (47e)

In a 3 l 3-neck flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel were placed 179 g of crude sodium enolate 46 dissolved in 1.4 l of absolute EtOH. After adding 73.0 g (0.427 mol) of benzyl bromide over a 1 hr period, the reaction mixture was refluxed with gentle stirring for 4 days. The reaction had progressed very little, as indicated by the fact that when a few drops of the mixture were shaken with several milliliters of ether and H_2O, the coloration was mostly in the water layer. An additional 50 g of benzyl bromide (123 g total, 0.719 mol) were placed in the reaction mixture, and refluxing was continued for another 6 days. The ether-water test then gave a positive result, with coloration mostly in the ether layer. The reaction mixture consisted of a dark red-black solution over some pink precipitate. The reaction flask was fitted for simple distillation, and, with the continued use of the mechanical stirrer, distillation was performed up to a boiling point of 130°/15 mm. This removed the EtOH and most of the unreacted benzyl bromide. The red-brown residue, a mixture of solid and liquid, was dissolved in 250 ml of water and 250 ml of ether. After extracting 3 times with ether, the combined extracts were washed with 8 portions of aqueous Na_2CO_3 solution. The ether solution was separated from the small amount of solid sludge that formed, and was then washed 3 times with aqueous NaCl solution. The 900 ml of ether solution were dried over $MgSO_4$, and removal of solvent in vacuo yielded 162 g of red-brown, opaque oil. Fractional distillation was performed, and the fraction boiling at or below 50°/0.1 mm was discarded. The desired product was collected in the following bp range: 93°/0.12 mm to 140°/0.05 mm. (The bp stabilized at 118°-120°/0.05 mm for a while.) This orange-yellow distillate crystallized in the condenser and the receiving flask, and a heat gun was used to prevent clogging the apparatus. The solid was recrystallized from hexane, yielding 61.8 g (34.3% based on benzyl bromide) of creamy-white crystals: mp 78-79° (lit.[50] mp 78-79°): nmr ($CDCl_3$) δ1.37 (s, 3H), 3.13 (s, 2H), 6.89 (s, 5H), 7.45-7.85 (m, 4H); ir (solid film, NaCl): 2990 (w), 2870 (w), 1740 (s), 1710 (s), 1580 (m), 1485 (m), 1440 (m), 1360 (m), 1325 (m), 1260 (s), 988 (s), 797 (m), 760 (s), 727 (m), 705 (s); mass spectrum m/e (rel intensity) 250 (41.3, M^+), 235 (41.0), 232 (11.7), 207 (12.0), 104 (16.9), 92 (10.0), 91 (100), 76 (11.7), 65 (11.1); exact mass--calcd. for $C_{17}H_{14}O_2$: 250.09930, found: 250.09931.

2-Benzyl-2-methyl-1,3-indandiol (49e)

A 1 l 3-neck flask, equipped with a mechanical stirrer, a dropping funnel, a reflux condenser, and a drying tube, was flushed with a stream of N_2 for 1 hr. In the flask were placed 9.0 g (0.24 mol) of powdered $LiAlH_4$ and 120 ml of anhydrous ether. A solution containing 30.0 g (0.120 mol) of indandione 47e in 375 ml of anhydrous ether was dropped into the stirred reducing agent over a 3 hr period. After half of hte substrate solution was added, the solid particles in the reaction mixture clumped together into a gray and white ball, except for some solid sticking to the vessel walls. Several gray balls of solid existed at the end of the addition period, and 250 ml of ether were added in an unsuccessful attempt to disperse the solids. The mixture was refluxed for 40 hr, but the heating and stirring were interrupted twice in order to manually breakup the solid lumps. The usual Fieser[73] method was used to destroy the unreacted $LiAlH_4$, resulting in a white precipitate. The solid was filtered off and washed well with ether. The combined ether solutions were dried over Na_2SO_4, and removal of solvent under vacuum yielded 30.8 g (99%) of an almost colorless, clear semisolid. After refrigeration, the crude product became a glassy solid, mp 43-51°. An attempt to dissolve the crude glass in ether resulted in a crystalline product, mp 66-92°. The diol did not need to be purified for use in the next reaction. Nmr ($CDCl_3$): δ0.48-0.94 (m, 3H), 1.96 (broad s, 2H), 2.62-3.24 (m, 2H), 4.22-5.17 (m, 2H), 6.97-7.54 (m, 9H); ir (solid film, NaCl): 3310 (b, s), 2980 (m), 2880 (m), 1600 (m), 1485 (m), 1445 (s), 1060 (m), 1020 (s), 750 (s), 705 (s).

1,3-Dibromo-2-benzyl-2-methylindane (50e)

A 250 ml 3-neck flask, equipped with a mechanical stirrer, a dropping funnel, a reflux condenser, and a drying tube, was flushed well with N_2. In the flask were placed 23.4 g (0.0864 mol) of PBr_3 and 100 ml of $CHCl_3$. A solution containing 10.0 g (0.0394 mol) of diol 49e in 50 ml of $CHCl_3$ was added to the PBr_3 solution during a 2 hr period. The reaction mixture was refluxed with stirring for 32 hr, and a bright orange coating developed on the flask walls. The reaction mixture was worked up the same way that crude dibromide 50d was isolated, except that the volume of water initially added to the reaction mixture was 15 ml. A clear, slightly viscous, light tan oil was obtained, and this crude product weighed 14.9 g (99.3%). The dibromide seemed to decompose slightly upon distillation (bp 152-158°/0.1 mm), so this method of purification was avoided. The crude product proved to be of adequate purity for the next reaction: nmr ($CDCl_3$): δ0.87-1.40 (m, 3H), 2.55-3.48 (m, 2H), 5.05-5.37 (m, 2H), 7.06-7.50 (m, 9H); ir (CCl_4, KBr cells): 3065 (m), 3030 (m), 2980 (m), 2930 (m), 1600 (m), 1490 (s), 1460 (s), 1450 (s), 1380 (m), 1235 (m), 1190 (s), 850 (m), 700 (s), 655 (m), 530 (m); mass spectrum m/e (rel intensity)(no parent peak) 220 (27.4, M^+-2Br), 219 (30.6), 218 (13.8), 204 (11.0), 203 (18.5), 202 (21.0), 129 (52.4), 128 (29.6), 92 (40.0), 91 (100).

Dimethyl-7-benzyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (51e)

The apparatus was identical to that used in the synthesis of diester adduct 51d. The procedure for carrying out the reaction and isolating the product was essentially the same as that used in the preparation of adducts 51b and 51d. In the flask were placed 20 ml of dry DMF and 7.5 g of new Zn-Cu couple. The solution that was added to the couple contained 6.8 g (0.018 mol) of dibromoindane 50c, 7.8 g (0.053 mol) of dimethyl azodicarboxylate, and 30 ml of dry DMF. The 160 ml of combined ether extracts, yellow and clear, were washed 3 times with aqueous NaCl solution. As the last traces of solvent were removed on the rotary evaporator, the residue tended to foam up, filling the flask. The foaming eventually stopped, leaving a clear, pale yellow, glassy residue: crude mp 58-65°. The solid product weighed 6.0 g (91%), and was pure enough for use in the next reaction: nmr ($CDCl_3$): δ0.90-1.46 (m, 3H {includes a large single peak at δ1.18}), 2.30 (s, 2H), 3.75 (d, 6H, in which one peak is much taller than the other), 4.84-5.27 (m, 2H), 6.80-7.76 (m, 9H); ir (NaCl): 2990 (m), 2910 (m), 1750 (s), 1710 (s), 1600 (w), 1485 (m), 1430 (s), 1325 (b, s), 1220 (s), 1125 (m), 760 (s), 705 (m); mass spectrum m/e (rel intensity) 366 (1.7, M^+), 307 (24.5), 291 (11.3), 275 (18.0), 219 (10.6), 202 (19.1), 189 (20.6), 129 (31.7), 91 (100), 59 (25.5); exact mass--calcd. for $C_{21}H_{22}N_2O_4$: 366.15780; found: 366.15778.

7-Benzyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38e)

The apparatus was the same as that used in the synthesis of azoxy compound 38a. The procedure for this two-step reaction sequence was very similar to those followed in the preparation of azoxy compounds 38a, 38b, and 38d. After placing 4.0 g (0.071 mol) of KOH pellets in the solid addition tube, an argon atmosphere was placed in the apparatus. The 4.1 g (0.011 mol) of diester adduct 51e were only partially soluble in 80 ml of absolute EtOH, and the mixture was placed in the reaction vessel. After flushing the mixture well with argon, it was heated to reflux, and the solid substrate dissolved. The pale yellow solution quickly turned to a gold color as the KOH was added. When 4 hr of refluxing and vibromixing were completed, there was some off-white precipitate coating the vessel walls or in suspension. The evaporated EtOH was replaced, via syringe, and the argon flow rate was approximately tripled. While the reaction vessel was surrounded by a water bath, 14 ml of 90% H_2O_2 were slowly dropped into the reaction mixture. (Nine ml were added in the evening, and 5 ml during the next morning. The total addition time was 12 hr.) Separation of the mixture occurred when the vibromixer was stopped with ca. 80 ml of yellow solution over 5 ml of a tan liquid. Extraction was done with 4 portions of CH_2Cl_2, giving 300 ml of a yellow-green organic solution. After drying the solution over $MgSO_4$, solvent removal under vacuum yielded 3.3 g of a tan, very viscous oil or semisolid. The crude product was chromatographed on a column containing 110 g of 80-200 mesh Al_2O_3, and CH_2Cl_2 was the first eluting solvent. No significant amount of azoxy compound eluted until just after the most yellow part of the first band came off the column. At this point, two fractions rich in azoxy compound were collected as slightly yellow solutions. (The second band material was still in the middle of the column.) Removal of solvent from the two azoxy fractions resulted in semisolids, and ir spectra indicated that their major component was the desired product. Each azoxy residue was triturated with five portions of n-pentane, yielding 0.81 g (28%) of a white powder: mp 122-124° (with slight gas evolution and decomposition): nmr ($CDCl_3$): δ1.28 (s, 3H), 2.36 (s, 2H), 5.01 (d, 1H), 5.10-5.38 (m, 1H), 6.69-7.74 (m, 9H); ir (solid film, NaCl): 3070 (w), 3040 (m), 2950 (w), 1605 (w), 1515 (s), 1465 (m), 1350 (w), 1215 (m), 765 (s), 740 (m), 708 (s); mass spectrum <u>m/e</u> (rel intensity)(no parent peak) 234 (2.0, M^+-NO), 220 (27.8, M^+-N_2O), 205 (3.7), 129 (46.9), 128 (21.0), 115 (5.8), 91 (100); exact mass--calcd. for $C_{17}H_{16}$ (M^+-N_2O): 220.12510; found: 220.12563.

Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.13; H, 6.14; N, 10.54.

Product Studies of Thermolysis Reactions

Columns Used for Qualitative, Quantitative, and Preparative Gas Chromatography, Involving the Products of the Thermolyses

Column A: 1/8 in X 8 ft 3% FFAP, on 60/80 mesh Chromosorb P.

Column B: 1/8 in X 9 ft 5% FFAP, on 60/80 mesh Chromosorb P.

Column C: 1/4 in X 10 ft 5% FFAP, on 60/80 mesh Chromosorb P.

Column D: 1/4 in X 10 ft 20% Apiezon L, on Chromosorb W (acid washed), 60/80 mesh.

Column E: 1/4 in X 5 ft 18% DC-200, on 60/80 mesh Chromosorb P.

Column F: 1/4 in X 15 ft 18% DC-200, on 60/80 mesh Chromosorb P.

Column G: 1/4 in X 18 ft 20% SE-30, on Chromosorb W.

Column H: 1/4 in X 8 ft 3% FFAP, on Chromosorb P.

Thermolyses of Azoxy Compound 38a

Azoxy compound 38a, which has two methyl substituents, was thermolyzed in benzene solution in sealed pyrex tubes (except for the reaction in cumene, described below). Tubes suitable for sealing were dried in an oven, and then flushed with nitrogen, prior to introduction of the sample. In a typical reaction, 50 mg (2.7×10^{-4} mol) of 38a were dissolved in 2 ml of benzene and placed in the tube. After the addition of another 3 ml of benzene, in order to wash down the inner walls of the tube, the resultant solution had an average azoxy concentration of 0.05M. The tubes were then flushed well with a stream of N_2, and sealing was done under N_2, at atmospheric pressure. Thermolyses were performed by heating the sample tubes in an oil bath. After each tube was opened, the solvent was removed under vacuum, usually leaving a clear yellow liquid as the product mixture.

Concerning all of the thermolyses performed on azoxy 38a, the benzene solutions ranged in concentration from 0.02M to 0.08M, and the reaction conditions varied from 180° (for 0.5 hr) to 204° (for 1.33 hr).

For glpc analyses, the crude product mixtures from the thermolyses of 38a were usually dissolved in small quantities of benzene or carbon tetrachloride (CCl_4), giving approximately 25-50% (V/V) solutions. (Warning--carbon tetrachloride was found to be corrosive to thermal conductivity detectors at detector temperatures above 150°.)

A series of thermolyses were performed on 0.05M solutions of 38a in order to determine yield and product ratio data.

Reaction A

A 0.05M solution containing 53 mg (2.8×10^{-4} mol) in 6 ml of benzene was thermolyzed at 180° for 3.0 hr. The crude product mixture was dissolved in 0.4 ml CCl_4 for nmr analysis. The spectrum showed only trace absorption within the δ4.90-5.50 region, which is where the bridgehead hydrogen signals of the azoxy starting material occur. The product mixture appeared to consist of less than 5% unreacted azoxy compound. The CCl_4 was then removed from the solution. In order to determine the percent yield of dimethylindene products via glpc analysis, 0.0273 g of mesitylene was added as an internal standard to the crude product mixture. This resultant solution was dissolved in benzene (25% V/V), and glpc analysis was carried out on column F at 158°, using a helium flow rate of 85 ml/min. Aside from the solvent and mesitylene peaks, the chromatogram consisted of two product peaks. The first product (component A) had a retention time of 15.2 min, and its peak area was 19 times larger than that of the second product (component B), which had a retention time of 20.5 min. These two components were collected and purified by preparative glpc, utilizing the same column and conditions. Their structures were determined from nmr, ir, and ms (including exact mass) data: component A was found to be 1,2-dimethylindene (25), and component B was 2,3-dimethylindene (26). The retention time of each compound was compared to those of the peaks in the original product mixture. Each pure product was injected separately, as a neat liquid or in benzene solution. The product identified as 25 gave rise to only one peak (aside from a solvent peak), with a retention time of approximately 15 min. The minor product, identified as 26, also showed only one peak on the chromatogram, and its retention time was 20.8 min. Two injections were made involving combinations or blends of different samples, containing one of the known, purified indene products and some of the crude thermolysis product mixture. In each case, one of the component peaks was enlarged, in comparison to its relative size in the chromatogram of the original product mixture itself. (The blend containing 25 enlarged the component A peak, and the blend containing 26 enlarged the B component peak.) Also, no additional peaks were observed. The glpc analyses of 25, 26, the blended samples, and the thermolysis product mixture were also performed on column D, at 166°; the same qualitative results were obtained as on column F.

The total yield of dimethylindenes, based on the sum of the peak areas of components A and B as compared to the area under the mesitylene peak, was 79%. Refer to Tables 9-12 for nmr, ir, and mass spectral data of 25 and 26.

Reaction B

A 0.05M solution containing 49 mg (2.6×10^{-4} mol) of 38a in 5 ml benzene was thermolyzed at 180° for 0.53 hr (32 min). After removal of benzene by rotary evaporation, the crude product mixture was dissolved in 0.5 ml of CCl_4 for nmr analysis. A lot of starting material, azoxy 38a, was still present, as evidenced by the significant nmr absorption within the δ4.90-5.50 region, due to the two bridgehead hydrogens of the azoxy compound. By comparing the integration of the signals of these azoxy bridgehead protons with the integration of the vinylic and benzylic proton absorptions of 25 and 26 in the mixture, the degree of reaction was estimated to be 41.4%. (This estimate corresponds to a half-life of about 40 min for 38a at 180°.) After removing the CCl_4, the crude product mixture was dissolved in a little benzene to form a solution for glpc analysis. As an internal standard, 0.0328 g of mesitylene was added. Using column F at 158°, with a helium flow rate of 85 ml/min, the ratio of 25 to 26 was determined to be larger than 50:1. The total indenes product yield was calculated to be 82%, based on the amount of azoxy compound that decomposed.

Reaction C

A 0.05M solution containing 41 mg (2.2×10^{-4} mol) of 38a in 4 ml of benzene was thermolyzed at 204° for 1.33 hr. In order to determine the percent yield of dimethylindenes, 0.0265 g of mesitylene was added to the crude product mixture. This resultant solution was dissolved in benzene (25% V/V), and gas chromatographed on column F at 158°, using a helium flow rate of 85 ml/min. Only two products were observed: indenes 25 and 26. The ratio of 25:26 in the product mixture was determined to be 1.9, and the total dimethylindene product yield was 78%.

Reaction D

A 0.05M solution containing 40 mg (2.1×10^{-4} mol) of 38a in 4 ml of benzene was heated at 204° for 0.5 hr. After removal of the solvent, 0.0356 g of mesitylene and about 10 drops of benzene were added to the crude product mixture. Gas chromatographic analysis on column F (at 158°, with a helium flow rate of 85 ml/min) indicated only two products: indenes 25 and 26. The ratio of 25:26 was 8.5, and the total yield of dimethylindenes was determined to be 82%.

Reaction E

When cumene was used as the solvent instead of benzene, 40 mg of azoxy 38a was placed in a pyrex tube with a total of 4 ml of cumene, giving a 0.05M solution. After sealing the tube under a nitrogen atmosphere, thermolysis was carried out at 180° for 3.0 hr. The usual work-up led to a liquid product mixture. Indene was chosen as the internal standard, since the mesitylene peak overlaps that of cumene on a gas chromatogram. For quantitative glpc analysis, 0.0472 g of indene was added to a 25% (V/V) benzene solution of the crude product mixture. Using glpc column F at 158°, the only two products observed for this reaction were indenes 25 and 26. Their yield was 79% , and the ratio of 25:26 was about 10.

Trapping of 2,2-Dimethylisoindene (24a) with Dimethyl Maleate

In a pyrex tube suitable for sealing were placed 41 mg (2.2×10^{-4} mol) of azoxy compound 38a dissolved in 2.0 ml of benzene. After adding 31 mg (2.2×10^{-4} mol) of dimethyl maleate, 2 ml of benzene were added in order to wash down the inner walls of the tube, making a 0.05M solution of each reagent. The tube was sealed under nitrogen and heated to 180° for 3 hr. The solvent was then removed in vacuo, and 1 ml of benzene was added to the residue. Gas chromatographic analysis on column G showed the presence of 1,2-dimethylindene (25) and indicated the only Diels-Alder product to be the endo-cis adduct 54, as demonstrated by authentic synthesis.

(See the next three experimental procedures, for alternative syntheses of 54.) The following yield data were obtained: 7.3 mg (12%) of adduct 54 and 2.2 mg of 1,2-dimethylindene (25). For 54, nmr (CCl_4): δ0.68 (s, 3H), 1.18 (s, 3H), 2.92-3.05 (m, 2H), 3.35 (s, 6H), 3.48-3.60 (m, 2H) 6.85-7.27 (m, 4H).

1,4-Dimethyl-1,4-endomethylene-tetralin-2,3-dicarboxylic Anhydride (28b)

In a 500 ml 3-neck flask fitted with a mechanical stirrer, a reflux condenser, and a dropping funnel were placed 35 ml of dry DMF and 18 g of Zn-Cu couple (freshly prepared from 20 mesh Zn by the method of LeGoff[51]). The procedure used in the reaction and for the isolation of product was the same as that involved in the synthesis of diester adduct 51a. A solution containing 11.8 g (0.0388 mol) of dibromide 50a, 7.6 g (0.078 mol) of maleic anhydride, and 45 ml of dry DMF was added to the Zn-Cu couple. The crude product weighed 3.7 g and was recrystallized from methanol (concentration and chilling of the solution were necessary). The purified yellow crystals weighed 1.73 g (18.4%): mp 114-115°; nmr ($CDCl_3$): δ0.81 (s, 3H), 1.20 (s, 3H), 3.27-3.45 (m, 2H), 3.83-3.97 (m, 2H), 7.20 (s, 4H).

Dimethyl endo,cis-7,7-dimethyl-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (54)

In a 50 ml boiling flask were placed 1.5 g (0.0062 mol) of anhydride 28b, 0.2 g of p-toluenesulfonic acid monohydrate, and 10 ml of absolute MeOH. The mixture was refluxed for 96 hr, after which 10 ml of toluene were added. The flask was then fitted for simple distillation, and a toluene-MeOH-water azeotrope was distilled at 65°/760 mm. Upon the addition of 10 ml of MeOH to the remaining mixture, refluxing was done for 24 hr. Azeotropic distillation was repeated, followed by the addition of another 10 ml of MeOH. After a final reflux period of 16 hr, one last azeotropic distillation was performed. The last traces of azeotrope were removed by vacuum distillation. The residual liquid was diluted with 25 ml of ether, washed with 10 ml of 3% Na_2CO_3 solution, and separated. The aqueous layer was extracted with 3 portions of ether. The combined ether solutions were then washed with water, and dried over $MgSO_4$. Solvent removal in vacuo resulted in pale yellow crystals, which were recrystallized from 50% aqueous EtOH. The yield of white crystals was 0.3 g (17%): mp 77-78°; nmr ($CDCl_3$): δ0.69 (s, 3H), 1.16 (s, 3H), 3.00-3.12 (m, 2H), 3.45 (s, 6H), 3.63-3.73 (m, 2H), 7.05-7.28 (m, 4H).

Method B (for preparing 54)

A solution containing 5.0 g (0.016 mol) of dibromoindane 50a and 4.7 g (0.033 mol) of dimethyl maleate in 25 ml of dry DMF was added to 8.5 g of freshly prepared Zn-Cu couple. The apparatus and procedure for this reaction were the same as for the synthesis of adduct 51a, except that a 250 ml 3-neck flask was used, and the excess of dimethyl maleate was removed by molecular distillation. Two recrystallizations from 50% aqueous EtOH yielded pale yellow crystals: mp 77.0-77.5°; nmr ($CDCl_3$): δ0.68 (s, 3H), 1.18 (s, 3H), 2.98-3.12 (m, 2H), 3.43 (s, 6H), 3.60-3.73 (m, 2H), 6.87-7.33 (m, 4H).

Trapping of 2,2-Dimethylisoindene (24a) with an Excess of Dimethyl Maleate

A solution containing 41 mg (2.2×10^{-4} mol) of azoxy 38a, 0.242 g (1.68×10^{-3} mol, or a 7.6-fold excess) of dimethyl maleate, and 4 ml of benzene was prepared for thermolysis. The solution, sealed in a pyrex tube under nitrogen, was heated at 185° for 4.5 hr. After removal of the solvent under vacuum, the residue was dissolved in 0.5 ml of CCl_4. The nmr spectrum indicated that the only Diels-Alder product was the endo-cis adduct 54, as demonstrated by authentic synthesis. There was no evidence of unreacted azoxy compound (38a). According to the integration, about 91% of the product mixture consisted of adduct 54, with only 7% of dimethylindene formed.

Trapping of 2,2-Dimethylisoindene (24a) with Dimethyl Fumarate

The thermolysis of 41 ml (2.2×10^{-4} mol) of azoxy compound 38a and 31 mg (2.2×10^{-4} mol) of dimethyl fumarate in 4 ml of benzene was carried out at 180° for 3.0 hr, in a pyrex tube sealed under N_2. After removing the benzene under vacuum, 1 ml of CCl_4 was added to the residue. Using column F at 158°, glpc analysis showed the presence of two rearrangement products: 1,2-dimethylindene (25) and 2,3-dimethylindene (26). Analysis on column G indicated that adduct 55 was the only Diels-Alder product, as demonstrated by authentic synthesis. The following yield data were obtained: 34 mg (54%) of adduct 55, 5.2 mg (16%) of 25, and 0.3 mg (0.9%) of 26. For 55, nmr (CCl_4): δ0.71 (s, 3H), 1.03 (s, 3H), 2.80 (d, 1H, J= 5 cps), 3.00-3.16 (m, 1H), 3.23-3.32 (m, 1H), 3.47 (s, 3H), 3.62-3.83 (m, 4H), 6.86-7.27 (m, 4H).

Dimethyl Trans-7,7-dimethyl-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (55)

The apparatus and procedure were the same as those involved in the synthesis of adduct 51a, except that a 250 ml reaction flask was used here. To 8.5 g of freshly prepared Zn-Cu couple were added 5.0 g (0.016 mol) of dibromoindane 50a and 3.6 g (0.025 mol) of dimethyl fumarate in 50 ml of dry DMF (dimethyl fumarate was only slightly soluble in DMF). The excess dimethyl fumarate was removed by crystallization in EtOH, and the solid product melted at 53-54°, after two recrystallizations from 50% aqueous EtOH. For 55, nmr ($CDCl_3$): 0.70 (s, 3H), 1.06 (s, 3H), 2.91 (d, 1H,, J = 5.5 Hz), 3.06-3.21 (m, 1H), 3.32-3.42 (m, 1H), 3.55 (s, 3H), 3.75 (s, 3H), 3.80-3.94 (m, 1H), 6.83-7.29 (m, 4H).

Gas Phase Pyrolysis of Azoxy Compound 38a

A flow pyrolysis apparatus was set up, consisting of a pyrex flask (used as a "sublimation pot"), a vycor pyrolysis tube inside of an electric furnace, pyrex connecting tubing covered with heating tape, and two consecutive collecting traps. One gram of azoxy 38a was placed in the sublimation pot, the traps were cooled to -78°, and the system was evacuated with a vacuum pump. The pyrolysis furnace was operated at 350°, while the heating tape was kept at 80° around the connecting tubing. Under a pressure of 0.15-0.20 mm, the azoxy compound was heated at 65-70° in the pot. Only a small amount of azoxy 38a sublimed or distilled into the 350° pyrolysis tube, over an 18 hr period. The volatile pyrolysate was collected in the first dry-ice trap, and was analyzed by nmr (in CCl_4 solution) and by glpc (using column F at 158°, with a helium flow rate of 85 ml/min). The pyrolysate was found to be a binary product mixture, consisting of indenes 25 and 26. Approximately 65% of this mixture was 2,3-dimethylindene (26). The solid that remained in the pot was unchanged (azoxy 38a) after the 18 hr heating period at 65-70°.

Thermolysis of Azoxy Compound 38b

Thermolysis of azoxy 38b (R's = ethyl, methyl) was done in benzene solution, contained in sealed pyrex tubes. Tubes suitable for sealing were dried in an oven, and then flushed with N_2, prior to introduction of the sample. In a typical thermolysis of the ethyl, methyl-azoxy compound, 100 mg (4.95×10^{-4} mol) of 38b were dissolved in 2 ml of benzene and placed in the pyrex tube. An additional 3 ml of benzene were used to wash down the inner walls of the tube. This azoxy solution, containing a total of 5 ml of benzene, had a concentration of 0.1M. The thermolysis tubes were sealed either under nitrogen at atmospheric pressure or under vacuum. In the latter case, the solution was degassed by performing three or four freeze-thaw cycles.

A typical thermolysis involved heating the sample tube in an oil bath at 190° for 4.0 hr, which caused 90% of the azoxy compound to react, losing N_2O. The reaction mixtures were typically clear, pale yellow solutions after thermolysis. Benzene was removed on the rotary evaporator, yielding a liquid that varied in color from yellow to light brown. (The amount of unreacted 38b was estimated from the nmr spectrum of the crude product mixture.)

The amount of azoxy 38b used in thermolytic runs ranged from 44 mg (in 4 ml of benzene) to 215 mg (in 6 ml of benzene). The concentrations of the various benzene solutions ranged from 0.05M to 0.2M. The thermolysis conditions varied from 187° (for 3.2 hr) to 200° (for 3.2 hr).

Gas Chromatographic Analysis of a Typical Product Mixture Obtained from the Thermolysis of Azoxy Compound 38b

The crude product mixture resulting from the thermolysis of 38b was dissolved in benzene, giving a 25-50% solution (V/V). Column C was heated to 128° for the analysis, and the helium flow rate was 20 ml/min. (A Varian Aerograph model 90-P gc was used.) The chromatogram consisted basically of four peaks and typical data are summarized in Table 3. (See Figure 4 for the appearance of a typical chromatogram.)

Table 3

Typical GLPC Data for the Product Mixture Obtained from the Thermolysis of 38b

Peak	Retention Time (min)	Relative Ratio of Peak Areas	% of Total Peak Area
Component A	34.0	24.3	72.6%
Component B	40.8	3.6	10.7
Component C	49.1	4.6	13.7
Component D	59.7	1.0	3.0

These four components were collected and purified by preparative glpc, utilizing the same column and conditions. Each component was gas chromatographed on column D at 160°, as well as on column C at 140°, in order to check for purity. In each case, just one peak appeared. After structure determination (using nmr, ir, ms {low resolution and exact mass}), the retention time of each compound was compared to those of the peaks in the original product mixture. Each purified component (having a known structure) was injected separately, on column C at 128°, as a neat liquid or in benzene solution.

Table 4

The Name and Retention Time of Each Component

Component	Name	Retention Time (min)
A	1-ethyl-2-methylindene (56a)	33.6
B	1-methyl-2-ethylindene (56b)	41.4
C	2-methyl-3-ethylindene (56c)	48.4
D	2-ethyl-3-methylindene (56d)	60.1

Four injections were made involving binary combinations (blends) of different samples, containing one of the known dialkylindenes with some of the thermolysis product mixture. In each case, one of the component peaks was enlarged, in comparison to its relative size in the chromatogram of the original product mixture itself. Also, no additional peaks were observed.

A very small fifth peak in the chromatogram of the thermolysis product mixture (less than 0.2% of the sum of all peak areas) represented the only other component. This substance was not isolated, though it had the same retention time (26.5 min) as 1,2-dimethylindene (25).

The use of vacuum instead of a nitrogen atmosphere during the thermolyses did not change the nature of the product mixtures.

The use of milder conditions (such as 187° for 3.2 hr) than those employed in the average thermolysis resulted in a product distribution favoring components A and B (see Figure 5). On the other hand, a higher than average thermolysis temperature (such as 200° for more than 3 hr) enhanced the amounts of components C and D relative to A and B (see Figure 6). Refer to Tables 9-12 for the nmr, ir, and mass spectral data of indenes 56a-d.

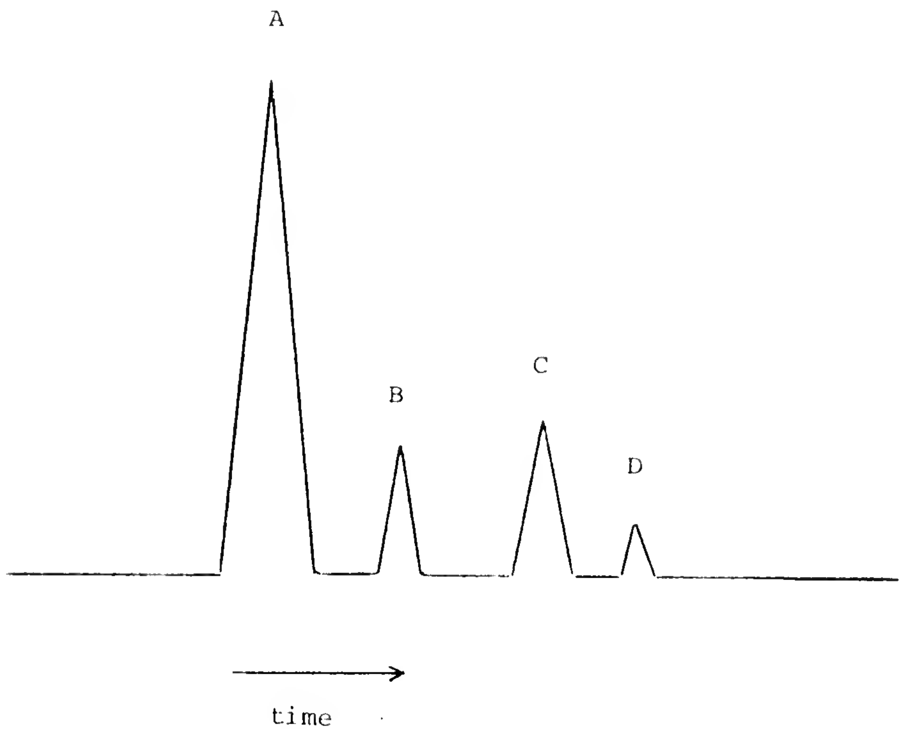


Figure 4: A typical chromatogram of the product mixture resulting from the average (190°, 4.0 hr) thermolysis of azoxy 38b

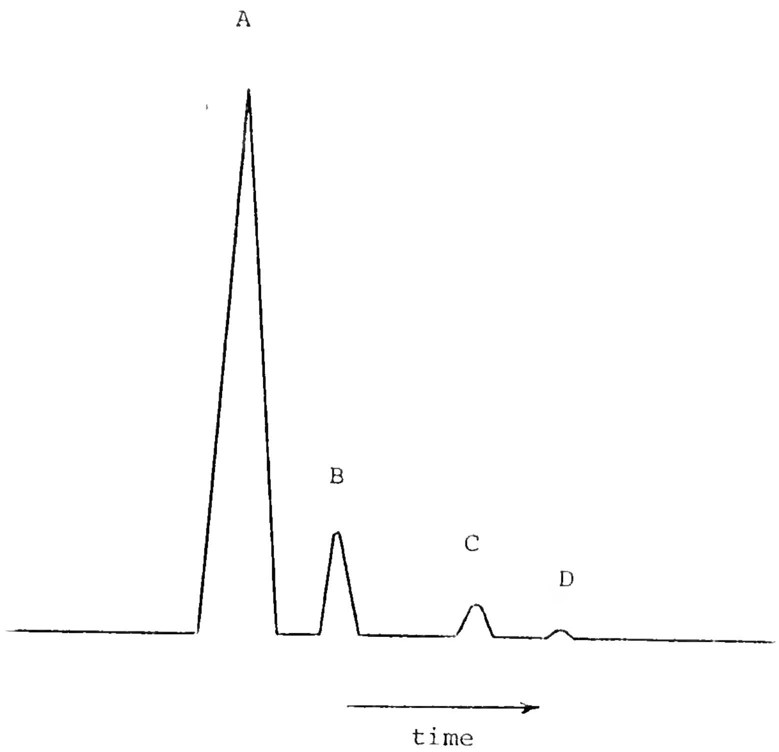


Figure 5: A chromatogram of the product mixture resulting from the thermolysis of 38b under relatively mild conditions

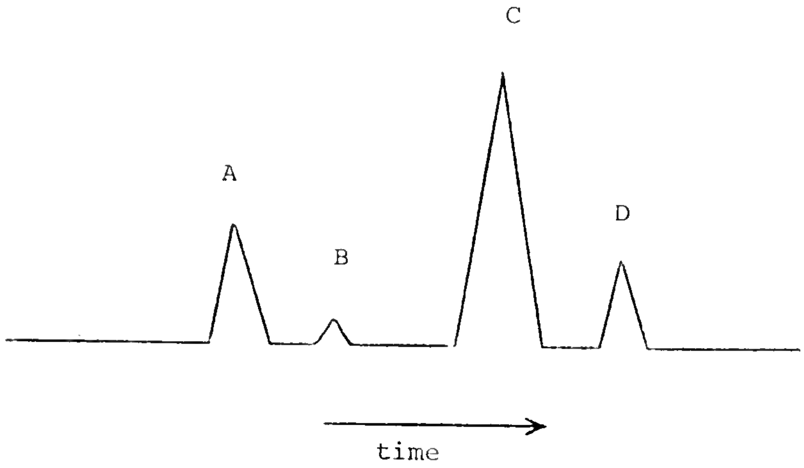


Figure 6: A chromatogram of the product mixture resulting from the thermolysis of 38b at 200° for several hours.

Relative Migratory Aptitude Determinations from Thermolyses of Azoxy 38b

Benzene solutions (25-50% V/V) of the product mixtures resulting from the thermolysis of azoxy 38b were analyzed on a Hewlett-Packard 5710A gas chromatograph. Several 1 μl injections were made for each product mixture studied. The relative peak areas of components A, B, C, and D were measured on each chromatogram, utilizing a digital integrator. The sum of the relative peak areas of components A and C, divided by the sum of the relative peak areas of components B and D, constituted the relative migratory aptitude.

$$\text{Relative Migratory Aptitude of Et:Me} = \frac{A + C}{B + D} = \frac{\underline{56a} + \underline{56c}}{\underline{56b} + \underline{56d}}$$

Product mixture 38b-1 was obtained from the thermolysis of 38b at 190° for 4.0 hr. Column A was heated at 120° for the analysis, and the carrier gas consisted of a 10 ml/min flow of nitrogen. The following values were obtained for the (A+C)/(B+D) ratio: 6.37, 6.44, and 6.41.

Product mixture 38b-2 resulted from the thermolysis of 38b at 190° for 4.0 hr (this was a more recent reaction than 38b-1). Column B was used at 120°, with a nitrogen flow rate of 10 ml/min. The relative migratory aptitude values obtained were 5.95, 5.88, 5.93, and 5.92.

Product mixture 38b-3 involved thermolyzing 38b at 200° for 3.2 hr. Column B was used at 120°, with the N_2 flow rate at 10 ml/min. The following ratios were obtained: 6.17, 6.30, 6.20, and 6.27.

Refer to Table 8 for a summary of relative migratory aptitude data.

Thermal Rearrangement of 1-Ethyl-2-methylindene (56a) to 2-Methyl-3-ethylindene (56c)

In a pyrex tube was placed a solution containing 33 mg of 1-ethyl-2-methylindene (component A) in 4 ml of benzene. After sealing the tube under N_2, the contents were heated at 200° for 25 hr. Solvent removal under vacuum left 29 mg of golden liquid. The crude product was dissolved in 5 drops of benzene, and glpc analysis was performed on column C, under the same conditions as before ($T = 128°$; He flow = 20 ml/min). There were two peaks, with retention times of 33.3 min and 48.9 min, and their relative peak areas were 1.0 to 9.0, respectively. The first component consisted of unreacted starting material (56a), and the major peak of longer retention time corresponded to component C of the product mixture from the thermolysis of azoxy 38b. This major product was collected by preparative glpc, and checked for purity on columns C and D (with column D at 160°). When injected together (as a blend) with the azoxy thermolysis product mixture on columns C and D, the component C peak was significantly enlarged, and no new peaks were observed. Its structure was assigned as 2-methyl-3-ethylindene (56c), on the basis of nmr and ir data.

Thermal Rearrangement of 1-Methyl-2-ethylindene (56b) to 2-Ethyl-3-methylindene (56d)

A solution containing 21 mg of 1-methyl-2-ethylindene (component B) in 4 ml of benzene was sealed in a pyrex tube under N_2. Thermolysis was done at 200° for 25 hr. After removing the solvent in vacuo, 18 mg of brown liquid were recovered. The crude product was dissolved in 5 drops of benzene, and glpc analysis on column C (at 128°, with a 20 ml/min helium flow) resulted in two peaks of significance. The first peak was the minor component, and its retention time of 41.6 min corresponded to the starting material (56b). The major peak occurred at 60.5 min, and it constituted 78% of the crude product. Using the same collection and analytical techniques employed in the rearrangement study of 56a to 56c, the structure of the major component was found to be that of the expected isomerization product, 2-ethyl-3-methylindene (component D of the azoxy thermolysis product mixture).

Trapping of 2-Ethyl-2-methylisoindene (24b) with Dimethyl Maleate

In a pyrex tube were placed 45 mg (2.2×10^{-4} mol) of ethyl, methyl-azoxy compound (38b) dissolved in 2 ml of benzene and 2.3 g (1.6×10^{-2} mol) of dimethyl maleate. Another 2 ml of benzene were added in order to wash down the inner walls of the tube. (An almost 75-fold excess of trapping reagent was employed.) The tube was sealed under vacuum, after degassing the solution. Thermolysis was carried out at 190° for 4.0 hr, after which the benzene was removed, using a rotary evaporator at aspirator pressure. The excess dimethyl maleate was removed by rotary evaporation at 0.3 mm, with heating to 70°. A dark tan, viscous oil resulted as the crude product mixture, weighing 59 mg. This mixture was dissolved in a little benzene, making a 33% solution, for gas chromatographic analysis. Column E was used at 172°, with a helium flow rate of 40 ml/min. The major component, having a retention time of 80 min, was collected and purified by preparative glpc. Its spectral data were consistent with the endo-cis diester adduct 57: nmr ($CDCl_3$): δ0.40-1.83 (complex, overlapping multiplets, 8H), 3.04-3.24 (narrow m, 2H), 3.47 (s, 6H), 3.57-3.82 (narrow m, 2H), 6.90-7.42 (m, 4H); ir (NaCl, neat): 3035 (w), 2975 (m), 2890 (w), 1755 (s), 1730 (s), 1465 (m), 1437 (m), 1350 (m), 1330 (m), 1248 (m), 1205 (s), 1190 (s), 1170 (s), 1052 (m), 748 (m); exact mass--calcd. for $C_{18}H_{22}O_4$: 302.15170, found: 302.15282.

The chromatogram of the product mixture also exhibited a set of four minor peaks, in the 7-10 min retention time range, with the first of these being much larger than the others. A sample of product mixture from the thermolysis of 38b itself (known to contain dialkylindenes 56a-d) was injected under the same glpc conditions, and a similar set of four peaks were exhibited on its chromatogram within the 7-10 min range. By comparing the peak areas of the apparent alkyl rearrangement products (56a-d) with that of the major product (57), it was estimated that 73% of the product mixture consisted of the endo-cis diester adduct (57).

Thermolysis of Azoxy Compound 38c

In a typical thermolysis of azoxy 38c (R's = cyclopropylcarbinyl, methyl), 130 mg (5.70 x 10^{-4} mol) of azoxy compound were placed in a pyrex tube with 13 ml of benzene, giving a 0.044M solution. Tube and sample preparation followed the same procedure as that involved in the thermolysis of 38b. Benzene solutions were degassed on the vacuum line, using three freeze-thaw cycles, and the tubes were then sealed under nitrogen. The thermolysis conditions were 180° for 3.0 hr, and the removal of benzene on the rotary evaporator left a tan liquid as the product mixture. All of the starting material (38c) had reacted, according to the nmr spectrum of the product mixture.

Gas Chromatographic Analysis of the Product Mixture Obtained from the Thermolysis of Azoxy Compound 38c

The crude product mixture resulting from the thermolysis of 38c was dissolved in 0.5 ml of benzene. Column H was used at 160° for the analysis, which indicated four components. Typical glpc data for this product mixture are shown in Table 5, and the chromatogram resembled the diagram in Figure 5.

Table 5

Typical GLPC Data for the Product Mixture Obtained from the Thermolysis of 38c

Peak	Retention Time (min)	Relative Ratio of Peak Areas	% of Total Peak Area
Component A	11.9	182	85.7%
Component B	14.2	23.0	10.8
Component C	17.6	6.4	3.0
Component D	20.1	1.0	0.47

These four components were collected and purified by preparative glpc, using column H at 160°, and their structures were determined. (See Tables 9-12 for the nmr, ir, and ms data of the products.) Establishing the purity of the components, and comparing their retention times with the thermolysis product mixture peaks, involved the same glpc techniques as those used to analyze the ethyl, methyl-indenes (56a-d). As a result, components A, B, C, and D were shown to be 1-cyclopropylcarbinyl-2-methylindene (58a), 1-methyl-2-cyclopropylcarbinylindene (58b), 2-methyl-3-cyclopropylcarbinylindene (58c), and 2-cyclopropylcarbinyl-3-methylindene (58d), respectively.

In order to confirm the absence of products containing an allylcarbinyl (3-butenyl) substituent (allylcarbinyl could result from the opening of the cyclopropylcarbinyl ring during thermolysis), the product mixture was compared with authentic samples of 1-(3-butenyl)-2-methylindene (59) and 2-methyl-3-(3-butenyl)indene (60). The syntheses of 59 and 60 are described in the following sections.

2-Methyl-1,3-indandiol (61)

In a 250 ml 3-neck flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser with a drying tube were placed

3.0 g (0.079 mol) of powdered $LiAlH_4$ and 50 ml of anhydrous ether. A solution containing 10.0 g (0.0625 mol) of 2-methylindane-1,3-dione (48) in 100 ml of anhydrous ether was dropped into the stirred reducing agent over a 1 hr period. The mixture was then refluxed for 24 hr, followed by the destruction of the excess $LiAlH_4$ at 0°, by the method of Fieser.[73] After removal of the precipitate, the ether solution was dried over $MgSO_4$. Removal of solvent under vacuum yielded 6.0 g (58%) of crude product, which was used in the next step without purification.

1-Bromo-2-methylindene (62)

In a 250 ml 3-neck flask equipped with a mechanical stirrer, a thermometer, a dropping funnel, and a drying tube was placed a solution containing 8.0 g (0.030 mol) of PBr_3, 1.0 g (0.013 mol) of dry pyridine, and 50 ml of anhydrous ether. In the dropping funnel was placed a solution of 6.0 g (0.037 mol) of diol 61 and 0.5 g (0.006 mol) of dry pyridine in 50 ml of anhydrous ether. The contents of the flask were cooled to -5° using an ice-salt bath, and stirring was begun. During a 2 hr period, the solution of diol was added in a dropwise manner, and the reaction mixture was kept in the temperature range of -5° to 0°. The reaction mixture was then stirred at room temperature for 24 hr. After the excess PBr_3 was destroyed by the addition of ice-water, the ether layer was separated and dried with $MgSO_4$. The ether was removed on a rotary evaporator, and the residue was found to consist mostly of 1,3-dibromo-2-methylindane. Dehydrobromination occurred upon distillation of this residual oil (some Na_2CO_3 was also placed in the distillation pot), yielding 1-bromo-2-methylindene: bp 86.0-87.5°/0.9 mm.

1-(3-Butenyl)-2-methylindene (59)

A 100 ml flask was equipped with a mechanical stirrer, a dropping funnel, a reflux condenser with a drying tube, and a nitrogen inlet tube.

After flushing the system with N_2, 0.6 g (0.003 mol) of 1-bromo-2-methylindene (62), 2.8 g (0.015 mol) of cuprous iodide, and 20 ml of anhydrous ether were placed in the flask. A solution containing 0.03 equivalents of 3-butenylmagnesium bromide (made from the Grignard reaction of 4-bromo-1-butene with magnesium) in 20 ml of anhydrous ether was added to the stirred suspension in the flask at room temperature, under a flow of N_2. The reaction mixture was then refluxed for 4 hr. After cooling to room temperature, 50 ml of water were added, and the organic layer was separated. The ether solution of product was dried over $MgSO_4$, and the solvent was removed on the rotary evaporator. For product 59: nmr ($CDCl_3$): δ1.47-2.27 (m, 7H), 3.15-3.44 (m, 1H), 4.70-5.23 (m, 2H), 5.44-6.16 (m, 1H), 6.35-6.55 (narrow m, 1H), 6.87-7.47 (m, 4H).

2-Methyl-3-(3-butenyl)indene (60)

In a pyrex tube was placed a solution containing 11 mg of 59 and 5 ml of benzene. The solution was degassed, and the tube was sealed under nitrogen. Thermolysis was performed at 190-195° for 20 hr. Solvent was removed in vacuo, and the residue was analyzed by nmr and gas chromatography, indicating essentially complete conversion of 59 to 60.

Gas Chromatographic Comparison of the 38c Thermolysis Product Mixture with Indene 59

Using the same conditions as for the previous analysis of the 38c thermolysis product mixture (column H at 160°), 1-(3-butenyl)-2-methylindene (59) was gas chromatographed, and it exhibited a retention time of 9.8 min. When a blend of 59 and the thermolysis product mixture was injected, five peaks resulted. The first peak was shown to be 59, with the other four being cyclopropylcarbinyl, methyl-indenes 58a-d.

The Determination of Relative Migratory Aptitude from the Thermolysis of Azoxy 38c

The product mixture from the thermolysis of 38c, dissolved in 0.5 ml of benzene, was analyzed via glpc in the same manner that the ethyl, methyl-indenes (56a-d) were studied. The peak areas of components A-D (consisting of indenes 58a-d) were plugged into the formula (A+C)/(B+D) in order to obtain relative migratory aptitude values, for cyclopropylcarbinyl versus methyl.

Product mixture 38c-1, obtained from the thermolysis of 38c at 180° for 3.0 hr, was analyzed on column A at 160°. Values for the relative migratory aptitude averaged 7.85.

Thermal Isomerization of 1-Cyclopropylcarbinyl-2-methylindene (58a) to 58c

A solution containing 21 mg of 58a in 5 ml of benzene was degassed and sealed under a nitrogen atmosphere in a pyrex tube. Thermolysis was performed at 200° for 22 hr, followed by removal of solvent on a rotary evaporator. The residue was gas chromatographed on column H at 160°, indicating a 78% extent of reaction. Infrared and glpc retention time data proved that the sole product was 2-methyl-3-cyclopropylcarbinylindene (58c).

Thermal Isomerization of 1-Methyl-2-cyclopropylcarbinylindene (58b) to 58d

A solution containing 7 mg of 58b in 5 ml of benzene was thermolyzed, worked up, and analyzed as in the preceding section. The reaction mixture was shown to consist of 18% unreacted 58b and 82% isomerization product. Infrared and glpc retention time data indicated this product to be 2-cyclopropylcarbinyl-3-methylindene (58d).

Thermolysis of Azoxy Compound 38d

In a typical thermolysis of azoxy 38d (R's = isopropyl, methyl), 90 mg (4.2×10^{-4} mol) were dissolved in a total of 5 ml of benzene.

The resultant concentration was 0.08M. The procedure used was the same as that involved in the preparation of 38b for thermolysis. The tubes were sealed either under N_2 at 1 Atmosphere, or in vacuo, after degassing the solution. A typical thermolysis was carried out in an oil bath at 185° for 4.0 hr, resulting in the decomposition of approximately 95% of azoxy 38d. Solvent removal on a rotary evaporator yielded a clear liquid that was yellow, tan, or light brown. (The amount of unreacted 38d was estimated from the nmr spectrum of the crude product mixture.)

The amount of azoxy compound used in each of the thermolysis reactions of 38d varied from 18 mg (in 4 ml of benzene) to 169 mg (in 6 ml of benzene). Concentrations of the various benzene solutions ranged from 0.02M to 0.13M. The lowest thermolysis temperature was 178° (for 3.0 hr), and 201° (for 22 hr) was the highest.

Gas Chromatographic Analysis of the Product Mixture Obtained from the Thermolysis of azoxy compound 38d

The crude product mixture resulting from the thermolysis of 38d was dissolved in benzene, giving a 25-50% (V/V) solution. Column C was heated at 129° for the analysis, and the helium flow rate was 20 ml/min. The chromatogram consisted of four peaks, and typical glpc data for this product mixture are shown in Table 6. (The appearance of a typical chromatogram is similar to the diagram in Figure 5.)

Table 6

Typical GLPC Data for the Product Mixture Obtained from the Thermolysis of 38d

Peak	Retention Time (min)	Relative Ratio of Peak Areas	% of Total Peak Area
Component A	39.4	38.90	81.1%
Component B	45.2	6.60	13.8
Component C	55.3	1.47	3.06
Component D	63.5	1.00	2.08

These four components were collected and purified by preparative glpc, utilizing the same column and conditions. The structure of each component was determined. (See Tables 9-12 for nmr, ir, and ms data.) The techniques for establishing the purity of the components, and for comparing their retention times with the original product mixture peaks, were the same as those employed in the glpc analysis of the ethyl, methyl-indenes (56a-d). In this way, components A, B, C, and D were shown to be 1-isopropyl-2-methylindene (63a), 1-methyl-2-isopropylindene (63b), 2-methyl-3-isopropylindene (63c), and 2-isopropyl-3-methylindene (63d), respectively.

Product mixtures were apparently unaffected when thermolyses were carried out in a nitrogen atmosphere instead of under vacuum. The effect of the product distribution of milder or harsher reaction conditions, relative to the average thermolysis, paralleled the results in the ethyl, methyl-system (involving products 56a-d). For example, thermolysis of 38d at 200° for 20 hr gave a product mixture whose chromatogram resembles Figure 6.

Relative Migratory Aptitude Determinations from Thermolyses of Azoxy 38d

Benzene solutions (25-50% V/V) of the product mixtures resulting from the thermolyses of azoxy 38d were analyzed via glpc in the same manner that the ethyl,methyl-indenes (56a-d) were studied. The peak areas of components A-D were plugged into the formula (A+C)/(B+D) in order to obtain relative migratory aptitide values, for isopropyl versus methyl.

Product mixture 38d-1 was obtained from the thermolysis of 38d at 185° for 4.0 hr. Column A was heated at 120° for the analysis, with a nitrogen flow rate of 10 ml/min. The following values for relative migratory aptitude were found: 5.31, 5.38; 5.31, and 5.36.

Product mixture 38d-2 involved the thermolysis of 38d at 194° for 4.5 hr. Column B was used at 120°, with a nitrogen flow rate of 10 ml/min. The following values were determined for relative migratory aptitude: 5.28, 5.26, and 5.25.

Product mixture 38d-3 resulted from the thermolysis of 38d at 190° for 3.25 hr. Column B was operated at 120° for the analysis. The relative migratory aptitude values were 5.22, 5.17, 5.30, 5.14, 5.30, 5.16, and 5.09. Refer to Table 8 for a summary of relative migratory aptitude data.

Thermal Rearrangement of 1-Isopropyl-2-methylindene (63a) to 2-Methyl-3-isopropylindene (63c)

A solution containing 50 mg of 63a in 5 ml of benzene was degassed and sealed under vacuum in a pyrex tube. The solution was heated at 195° for 28 hr. Almost all of the solvent was removed by rotary evaporation, leaving enough benzene to make about 0.5 ml of product solution. Gas chromatographic analysis was performed on column C at 129°, using a helium flow rate of 21 ml/min. The product solution exhibited two peaks, other than benzene, with a 3:7 peak area ratio. The minor component had a retention time of 39.3 min, corresponding to unreacted starting material (63a). The major product was recorded at 54.3 min, correlating with component C of the product mixture from the thermolysis of 38d. Using the same preparative and analytical glpc techniques employed in the isomerization study of 56a to 56c, the major product was found to be 2-methyl-3-isopropylindene (63c). (The structural assignment was confirmed by comparative nmr and ir data.)

Thermal Rearrangement of 1-Methyl-2-isopropylindene (63b) to 2-Isopropyl-3-methylindene (63d)

A degassed solution of 20 mg of 63b in 4 ml of benzene was sealed under vacuum in a pyrex tube. Thermolysis was carried out at 200° for 24 hr. All but a few drops of benzene was removed from the product mixture, and the glpc conditions were the same as those used in the previous study (the isomerization of 63a to 63c). Analysis indicated a binary mixture: the minor component (10%) came off at 44.8 min, and the 90% product had a retention time of 61.7 min. The first peak exhibited the same glpc properties as the starting material (63b), and the major component correlated well with component D of the azoxy thermolysis product mixture. This product was collected and examined in the same way that product 56c was treated in the isomerization study of 56a to 56c. As a result, the isomerization product was found to be 2-isopropyl-3-methylindene (63d).

Thermolysis of Azoxy Compound 38e

A typical thermolysis of 38e (R's = benzyl, methyl) involved 50 mg (1.9×10^{-4} mol) of the azoxy compound dissolved in a total of 5 ml of benzene, giving a concentration of 0.04M. The preparation of the thermolysis sample involved the same procedure as described for 38b (tubes were sealed in vacuo or under N_2). The thermolysis conditions were typically 190° for 3.0 hr. The benzene was removed with a rotary evaporator, and the residual liquid product mixture ranged in color from yellow to light brown. The nmr spectrum of the product mixture indicated that almost all of the starting material (roughly 98%) had decomposed. Sample size among the various thermolyses of 38e ranged from 33 mg (in 5 ml of benzene) to 83 mg (in 5 ml of benzene). Azoxy concentrations ranged from 0.03M to 0.06M. Thermolysis conditions varied from 175° (for 3.2 hr) to 194° (for 3.75 hr).

Gas Chromatographic Analysis of the 38e Thermolysis Product Mixture

The crude product mixture was dissolved in a little benzene, giving a 25-50% (V/V) solution. The analysis was performed on column B at 180°, using a nitrogen flow rate of 12 ml/min. The chromatogram consisted of four peaks, and typical glpc data are shown in Table 7.

Table 7

Typical GLPC Data for the Product Mixture Resulting From the Thermolysis of 38e

Peak	Retention Time (min)	Relative Ratio of Peak Areas	% of Total Peak Area
Component A	29.2	214	83.26
Component B	33.3	4.16	1.62
Component C	39.5	37.9	14.73
Component D	47.1	1.00	0.389

Components A and C were collected and purified by preparative glpc, using column C at 180°, or column E at 165° (the helium flow rate was 22 ml/min for both columns). The structure of both components was determined. (See Tables 9-12 for nmr, ir, and ms data.) Establishing the purity of the components, and comparing their retention times with the peaks of the thermolysis product mixture, involved the same glpc techniques as those used to analyze indenes 56a-d. As a result, components A and C were found to be 1-benzyl-2-methylindene (64a) and 2-methyl-3-benzylindene (64c), respectively. Components B and D were not isolated or characterized, except by a combination gas chromatography-mass spectral (gc-ms) analysis of the product mixture. Components B and D were very scarce in the product mixtures, and the glpc retention time difference was relatively small between the very large component A and the small component B. As a result, the isolation of pure samples of B and D was an impractical task. Based on the identities of the other sets of indene products studied, the B and D components were believed to be 1-methyl-2-benzylindene (64b) and 2-benzyl-3-methylindene (64d), respectively. The gc-ms data indicated molecular weights of 220 for both, with a large peak at 129 and the base peak at 91 in each case.

Relative Migratory Aptitude Determinations from Thermolyses of Azoxy 38e

Benzene solutions of the 38e thermolysis product mixtures were analyzed via glpc in the same way that indenes 56a-d were studied. The peak areas were plugged into the formula (A+C)/(B+D) in order to obtain values of the relative migratory aptitude, for benzyl versus methyl. (The peak of component D (64d) was often too small for its area to be counted by the digital integrator. In such cases, the formula (A+C)/B was used.)

Product mixture 38e-1 was obtained from the thermolysis of azoxy 38e at 190° for 2.8 hr. Column A was used at 170° for the analysis, with a nitrogen flow rate of 21 ml/min. The following relative migratory aptitude values were found: 61.83, 60.52, 54.09, 64.94, and 56.67.

Product mixture 38e-2 resulted from the thermolysis of 38e at 175° for 3.2 hr. Column A was employed again at 170°. Relative migratory aptitude values determined were 51.10, 50.65, and 52.32.

Refer to Table 8 for a summary of relative migratory aptitude data.

Thermal Rearrangement of 1-Benzyl-2-methylindene (64a) to 64c

A solution containing 19 mg of 64a in 6 ml of benzene was sealed in a pyrex tube under a nitrogen atmosphere. It was thermolyzed at 201° for 34 hr, and the benzene was then removed on a rotary evaporator, leaving 18 mg of residue. When placed in a freezer overnight, the residue solidified. (This property was also observed for indene 64c.) Gas chromatographic analysis was performed on column B at 180°, using a nitrogen flow rate of 12 ml/min. Two non-solvent peaks were observed: a minor (30%) peak at 28.0 min, and a 70% peak at 40.8 min. The former correlated with the starting material (64a), while the latter exhibited the same retention time as component C (64c) of the azoxy thermolysis product mixture. This major component was collected and purified on glpc column E. Using the analytical techniques employed in the rearrangement study of 56a to 56c, the isomerization product was found to be 2-methyl-3-benzylindene (64c).

Table 8

Relative Migratory Aptitude of R vs Methyl

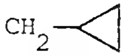
Thermolysis Product Mixture	R	Thermolysis Temp. (°C)	Thermolysis Time (hr)	Glpc Column	Glpc Temp. (°C)	Relative Ratio (Average) R/Me	Standard Deviation
38b-1	Et	190°	4.0	A	120°	6.41	0.04
38b-2	Et	190°	4.0	B	120°	5.92	0.03
38b-3	Et	200°	3.2	B	120°	6.24	0.06
38c-1		180°	3.0	A	160°	7.85	0.08
38d-1	i-Pr	185°	4.0	A	120°	5.34	0.04
38d-2	i-Pr	194°	4.5	B	120°	5.26	0.02
38d-3	i-Pr	190°	3.25	B	120°	5.20	0.08
38e-1	CH_2Ph	190°	2.8	A	170°	59.61	3.83
38e-2	CH_2Ph	175°	3.2	A	170°	51.36	0.86

Table 9

NMR Data for the Thermolysis Products

Compound	Solvent	Aromatic Protons (δ)	Vinylic Protons (δ)	Alkyl Protons (δ)
25	CCl_4 (60MHz)	6.86-7.42 (m, 4H)	6.34 (br.s, 1H)	1.26 (d, 3H), 2.04 (s, 3H), 3.14 (q, 1H)
26	CCl_4 (60MHz)	6.79-7.34 (m, 4H)	--	2.01 (s, 6H), 3.15 (s, 2H)
56a	$CDCl_3$ (60MHz)	6.95-7.49 (m, 4H)	6.44 (s, 1H)	0.60 (t, 3H), 1.60-2.27 (m, 5H), 3.27 (t, 1H)
56b	CCl_4 (60MHz)	6.87-7.40 (m, 4H)	6.25-6.47 (m, 1H, J = 1.5cps)	0.97-1.42 (m, 6H), 2.37 (q, 2H), 3.19 (q, 1H)
56c	$CDCl_3$ (60MHz)	6.92-7.59 (m, 4H)	--	1.16 (t, 3H), 2.06 (s, 3H), 2.55 (q, 2H) 3.27 (s, 2H).
56d	CCl_4 (60MHZ)	6.83-7.67 (m, 4H)	--	1.16 (t, 3H), 2.03 (s, 3H), 2.49 (q, 2H), 3.24 (s, 2H)
58a	$CDCl_3$ (100 MHz)	6.96-7.51 (m, 4H)	6.45 (s, 1H)	0.10-0.80 (m, 5H), 1.40-1.85 (m, 2H), 2.08 (s, 3H), 3.32 (t, 1H, J = 6 cps)
58b	$CDCl_3$ (100MHZ)	7.00-7.51 (m, 4H)	6.58 (s, 1H)	0.12-0.66 (m, 4H), 0.76-1.14 (m, 1H) 1.25 (d, 3H, J = 8cps), 2.30 (d, 2H, J = 7 cps), 3.35 (q, 1H, J = 8 cps)
58c	$CDCl_3$ (100MHZ)	6.98-7.42 (m, 4H)	--	0.08-0.55 (m, 4H), 0.78-1.16 (m, 1H) 2.04 (s, 3H), 2.51 (d, 2H, J = 7 cps), 3.26 (s, 2H)

continued

Table 9 Continued

Compound	Solvent	Aromatic Protons (δ)	Vinylic Protons (δ)	Alkyl Protons (δ)
58d	$CDCl_3$ (100MHz)	7.04-7.46 (m, 4H)	--	0.17-0.62 (m, 4H), 0.70-1.00 (m, 1H), 2.04 (s, 3H), 2.34 (d, 2H, J = 7cps), 3.40 (S, 2H)
63a	CCl_4 (60MHz)	6.78-7.47 (m, 4H)	6.40 (s, 1H)	0.59 (d, 3H), 1.15 (d, 3H), 1.87-2.63 (m, 4H), 3.14 (br. S, 1H)
63b	CCl_4 (60MHz)	6.87-7.37 (m, 4H)	6.33-6.47 (m, 1H)	1.23 (t, 9H), 2.68 (hept., 1H), 3.36 (q, 1H)
63c	CCl_4 (60MHz)	6.77-7.49 (m, 4H)	--	1.34 (d, 6H), 2.08 (s, 3H), 2.84-3.41 (m, 3H)
63d	CCl_4 (60MHz)	6.77-7.47 (m, 4H)	--	1.16 (d, 6H, J = 7cps), 2.04 (t, 3H, J = 2cps), 2.72-3.49 (m, 3H)
64a	$CDCl_3$ (60MHz)	6.72-7.62 (m, 9H)	6.30-6.57 (m, 1H)	2.08 (s, 3H), 2.37-2.97 (m, 1H), 3.06-3.97 (m, 2H)
64c	$CDCl_3$ (60MHz)	6.84-7.67 (m, 9H)	--	2.17 (s, 3H), 3.42 (s, 2H), 3.96 (s, 2H)

Table 10

Ir Data for the Thermolysis Products

Compound	Absorption bands in cm^{-1} (relative intensity)
25	3060 (m), 3025 (m), 2975 (s), 2940 (s), 2880 (m), 1630 (m), 1600 (w), 1465 (s), 1442 (s), 1372 (w), 1217 (w), 1018 (m), 871 (m), 841 (m), 779 (w), 754 (s), 740 (s), 612 (m)
26	3078 (w), 3055 (m), 3030 (m), 2980 (m), 2920 (s), 2890 (m), 2865 (m), 1635 (w), 1608 (w), 1470 (s), 1443 (m), 1398 (m), 1387 (m), 1227 (w), 1206 (w), 1020 (m), 759 (s), 730 (s)
56a	3060 (m), 3025 (m), 2975 (s), 2940 (s), 2875 (s), 1620 (m), 1605 (w), 1468 (s), 1447 (s), 1385 (m), 1023 (m), 880 (m), 852 (m), 812 (w), 757 (s), 738 (s), 663 (m), 640 (m)
56b	3070 (m), 3025 (m), 2975 (s), 2940 (s), 2885 (s), 1613 (m), 1467 (s), 1435 (m), 1373 (w), 1020 (m), 873 (m), 850 (m), 752 (s), 740 (s)
56c	3075 (m), 3045 (m), 3023 (m), 2975 (s), 2935 (s), 2880 (s), 1630 (m), 1605 (m), 1460 (s), 1440 (m), 1395 (s), 1373 (m), 1222 (m), 1203 (m), 1058 (m), 1021 (m), 760 (s), 720 (s)
56d	3075 (m), 3055 (m), 3030 (m), 2975 (s), 2940 (s), 2890 (s), 1630 (m), 1605 (m), 1470 (s), 1460 (m), 1440 (m), 1395 (m), 1385 (m), 1302 (m), 1206 (m) 1020 (m), 760 (s), 720 (s)
58a	3010, 2950, 2860, 1630, 1460, 1435, 1025, 940, 880, 840, 758, 745
58b	3010, 2900, 2850, 1620, 1455, 1040, 1020, 935, 843, 755, 740
58c	3010, 2940, 2860, 1450, 1020, 935, 830, 762, 732, 717
58d	3050, 2940, 1450, 1000, 755, 720
63a	3078 (m), 3055 (m), 3030 (m), 2970 (s), 2940 (s), 2880 (s), 1620 (m), 1602 (w), 1465 (s), 1441 (m), 1390 (m), 1371 (m), 1242 (w), 1027 (w), 848 (m), 804 (w), 757 (s), 734 (s), 660 (m), 631 (m)
63b	3072 (m), 3025 (m), 2975 (s), 2940 (s), 2880 (s), 1610 (w), 1526 (w), 1468 (s), 1384 (m), 1367 (m), 1269 (w), 1017 (m), 872 (m), 850 (m), 753 (s), 740 (s), 667 (m), 620 (m)
63c	3078 (w), 3050 (w), 3030 (m), 2975 (s), 2940 (m), 2882 (m), 1618 (w), 1603 (w), 1462 (s), 1397 (m), 1386 (m), 1364 (w), 1057 (w), 1028 (w), 768 (s), 723 (s)

Table 10 continued

Compound	Absorption bands in cm^{-1} (relative intensity)
63d	3075 (w), 3050 (w), 3028 (w), 2975 (s), 2938 (m), 2880 (m), 1625 (w), 1607 (w), 1470 (m), 1397 (m), 1388 (m), 1363 (w), 1314 (w), 1209 (m), 1017 (m), 760 (s), 722 (s)
64a	3095 (w), 3075 (m), 3037 (m), 2920 (m), 2860 (m), 1618 (w), 1605 (m), 1497 (m), 1467 (s), 1457 (s), 1440 (m), 1382 (w), 1080 (w), 1035 (w), 1022 (m), 840 (m), 753 (s), 733 (m), 702 (s)
64c	3095 (w), 3075 (m), 3035 (m), 2920 (m), 2880 (w), 1630 (w), 1605 (m), 1498 (m), 1470 (m), 1457 (m), 1395 (m), 1077 (w), 1030 (w), 775 (m), 757 (s), 720 (s), 700 (m)

Note: All spectra were performed on neat liquids, using NaCl plates

Table 11

Mass Spectral Data for the Thermolysis Products

Compound	Major Peaks (relative intensity)
25	144 (55.7, M^+), 130 (10.7), 129 (100), 128 (45.2), 127 (14.7), 115 (11.3)
26	144 (59.6, M^+), 143 (11.1), 130 (10.7), 129 (100), 128 (42.9), 127 (13.8), 115 (13.8)
56a	158 (49.5, M^+), 144 (12.3), 143 (100), 141 (14.0), 130 (11.3), 129 (56.6), 128 (63.7), 127 (17.2), 115 (14.8)
56b	158 (45.1, M^+), 144 (12.6), 143 (100), 141 (15.9), 129 (36.4), 128 (49.6), 127 (12.2), 115 (15.6)
56c	158 (45.9, M^+), 144 (12.6), 143 (100), 142 (10.2), 141 (25.5), 129 (50.4), 128 (77.2), 127 (19.0), 115 (30.0)
56d	158 (47.7, M^+), 144 (12.1), 143 (100), 141 (14.5), 129 (34.1), 128 (51.9), 127 (11.7), 115 (15.7)
58a	184 (67.3, M^+), 169 (19.2), 143 (100), 142 (32.9), 141 (34.1), 129 (79.8), 128 (90.5), 127 (28.2)
58b	184 (58.9, M^+), 169 (32.6), 155 (27.0), 143 (100), 142 (31.3), 141 (40.6), 130 (20.0), 129 (90.7), 128 (73.8), 115 (23.5)
58c	184 (67.7, M^+), 169 (20.4), 143 (100), 142 (34.8), 141 (43.8), 129 (73.5), 128 (89.7), 115 (25.0)
58d	184 (62.8, M^+), 169 (32.2), 155 (25.7), 143 (100), 142 (31.3), 141 (38.7), 130 (20.1), 129 (83.7), 128 (71.5), 127 (20.1), 115 (25.0)
63a	172 (47.2, M^+), 158 (12.8), 157 (100), 142 (31.9), 141 (20.1), 130 (62.7), 129 (97.0), 128 (56.9), 127 (21.2) 115 (43.4), 44 (23.0), 43 (19.0)
63b	172 (34.6, M^+), 158 (13.1), 157 (100), 142 (20.9), 141 (15.6), 130 (22.7), 129 (52.2), 128 (22.7), 115 (18.0) 43 (4.0)
63c	172 (52.4, M^+), 158 (13.2), 157 (100), 155 (15.3), 143 (10.9), 142 (41.8), 141 (30.2), 130 (49.9), 129 (81.0) 128 (40.8), 127 (14.3), 115 (44.1), 44 (19.4), 43 (19.1)

continued

Table 11 continued

Compound	Major Peaks (relative intensity)
63d	172 (36.7, M^+), 158 (13.0), 157 (100), 142 (16.1), 141 (15.3), 130 (20.6), 129 (42.4), 128 (20.8), 115 (14.7), 43 (4.1)
64a	220 (46.2, M^+), 205 (6.8), 129 (68.5), 128 (30.4), 127 (11.1), 91 (100)
64c	220 (53.9, M^+), 205 (7.8), 130 (10.0), 129 (71.0), 128 (26.0), 91 (100)

Table 12

Exact Mass Data for the Thermolysis Products

Compound	Formula	Exact Mass	Theoretical Mass
25	$C_{11}H_{12}$	144.09358	144.09390
26	$C_{11}H_{12}$	144.09296	144.09390
56a	$C_{12}H_{14}$	158.10877	158.10950
56b	$C_{12}H_{14}$	158.10933	158.10950
56c	$C_{12}H_{14}$	158.10983	158.10950
56d	$C_{12}H_{14}$	158.10926	158.10950
58c	$C_{14}H_{16}$	184.12535	184.12510
63a	$C_{13}H_{16}$	172.12558	172.12510
63b	$C_{13}H_{16}$	172.12511	172.12510
63c	$C_{13}H_{16}$	172.12564	172.12510
63d	$C_{13}H_{16}$	172.12509	172.12510
64a	$C_{17}H_{16}$	220.12491	220.12510
64c	$C_{17}H_{16}$	220.12531	220.12510

APPENDIX

NMR AND IR SPECTRA OF RELEVANT COMPOUNDS

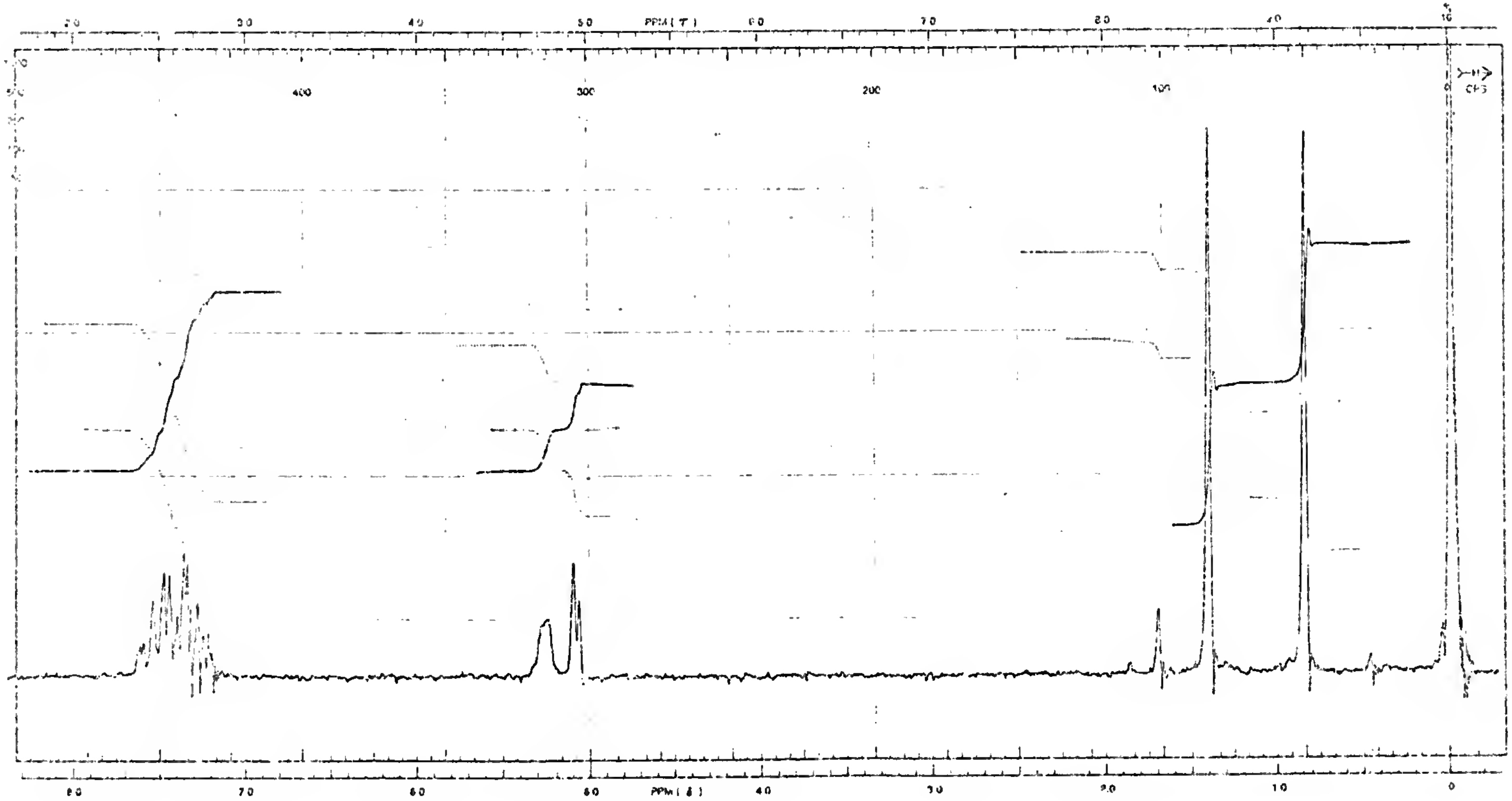


Figure A-1: Nmr of 7,7-dimethyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (<u>38a</u>)

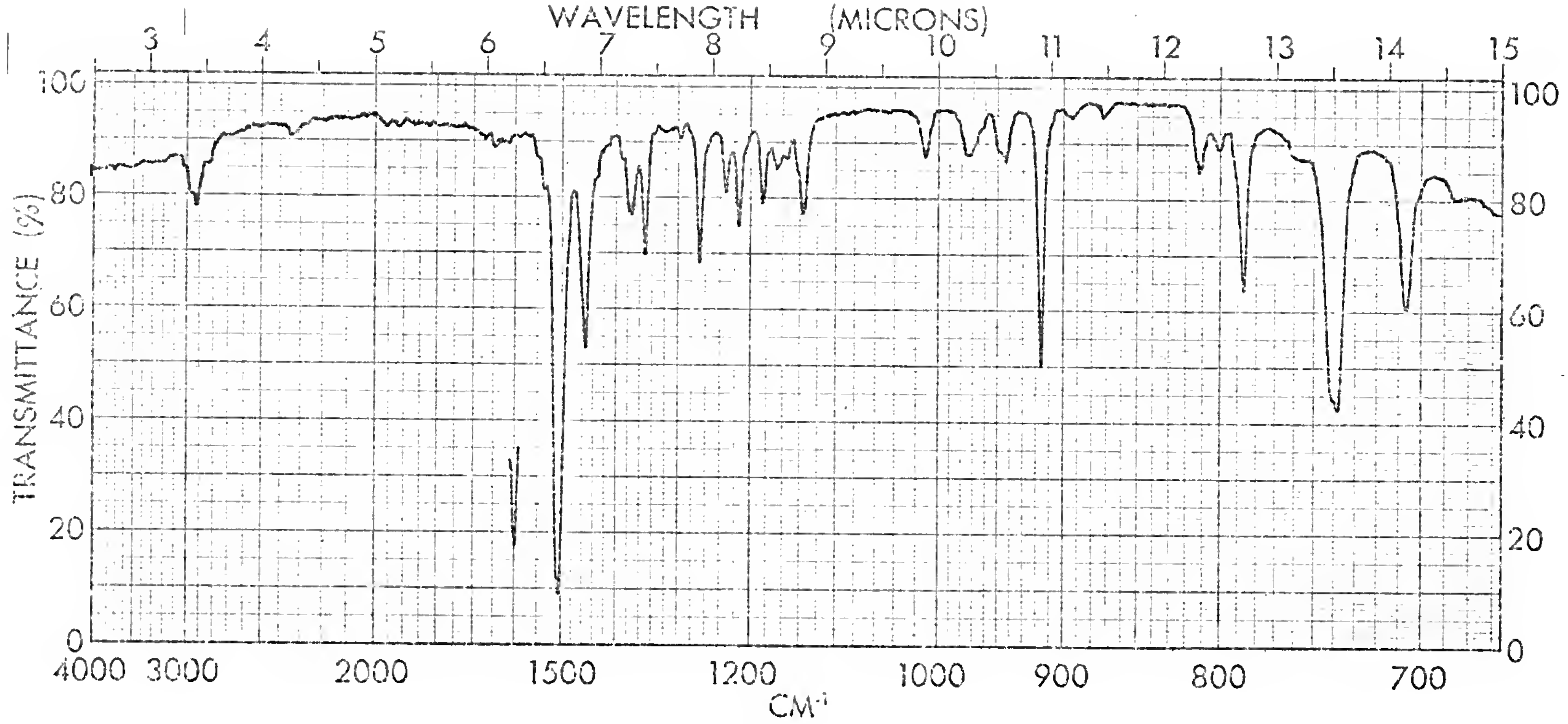


Figure A-2: Ir of 7,7-dimethyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38a)

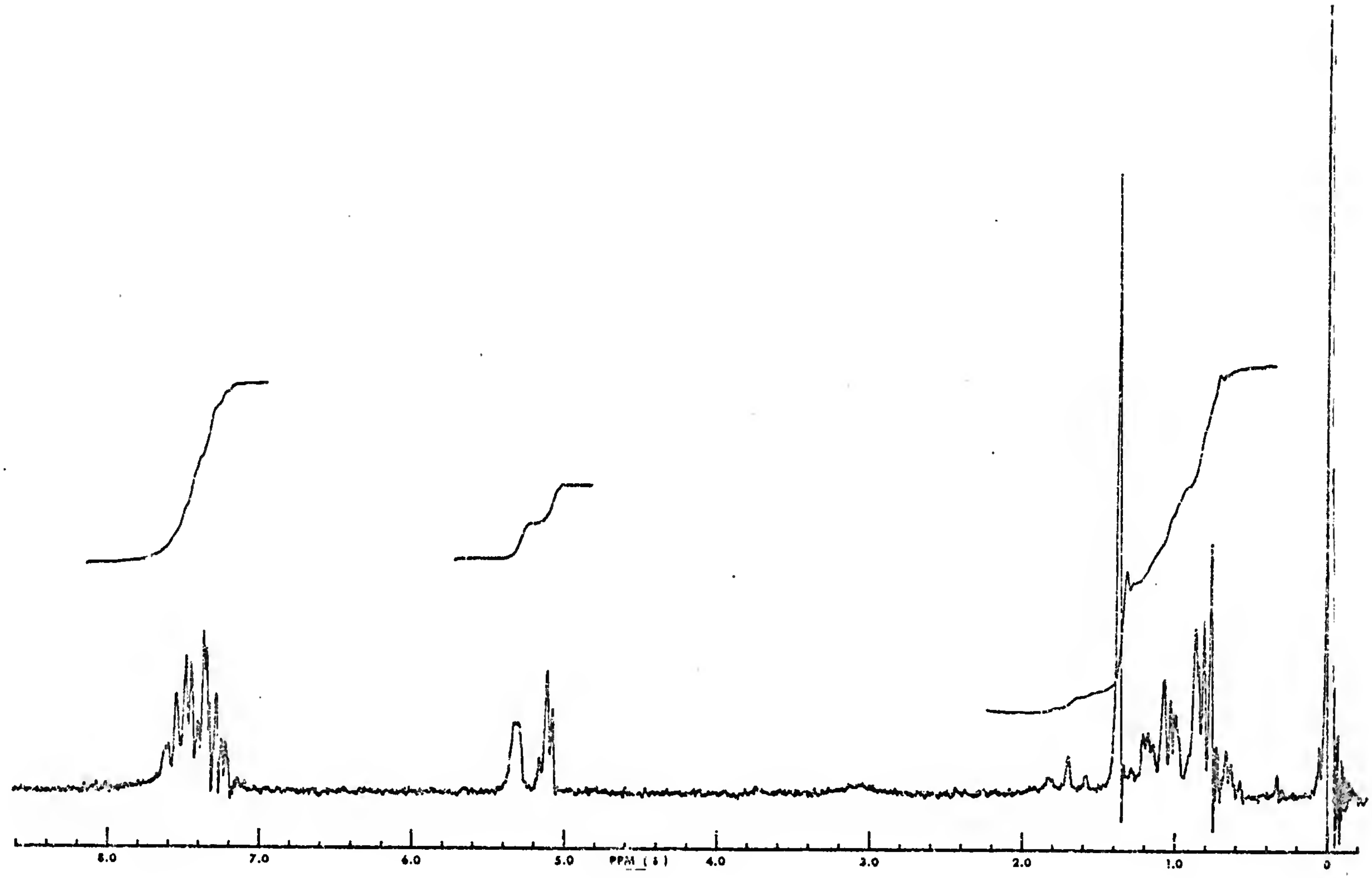


Figure A-3: Nmr of 7-ethyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (<u>38b</u>)

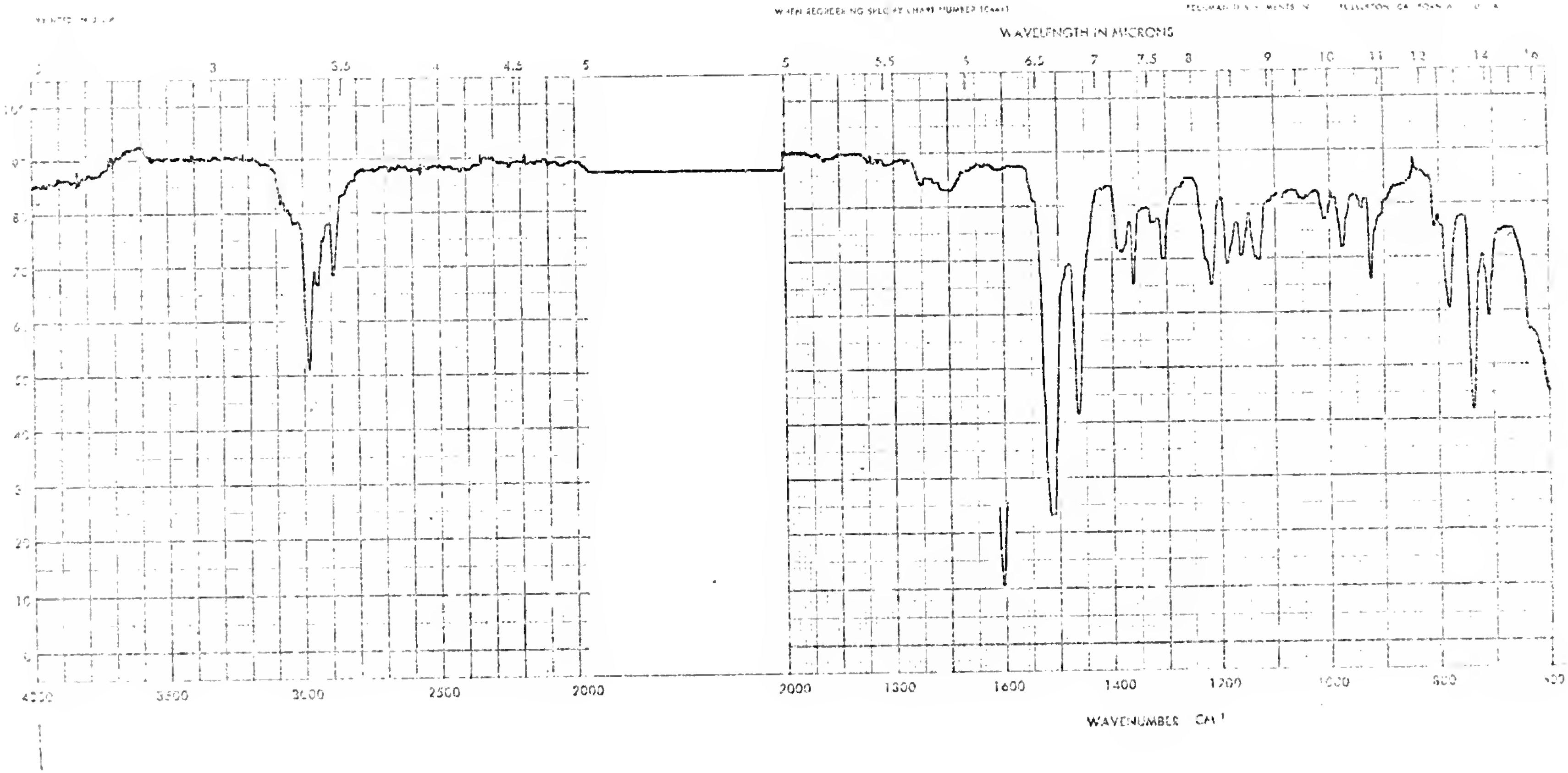


Figure A-4: Ir of 7-Ethyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38b)

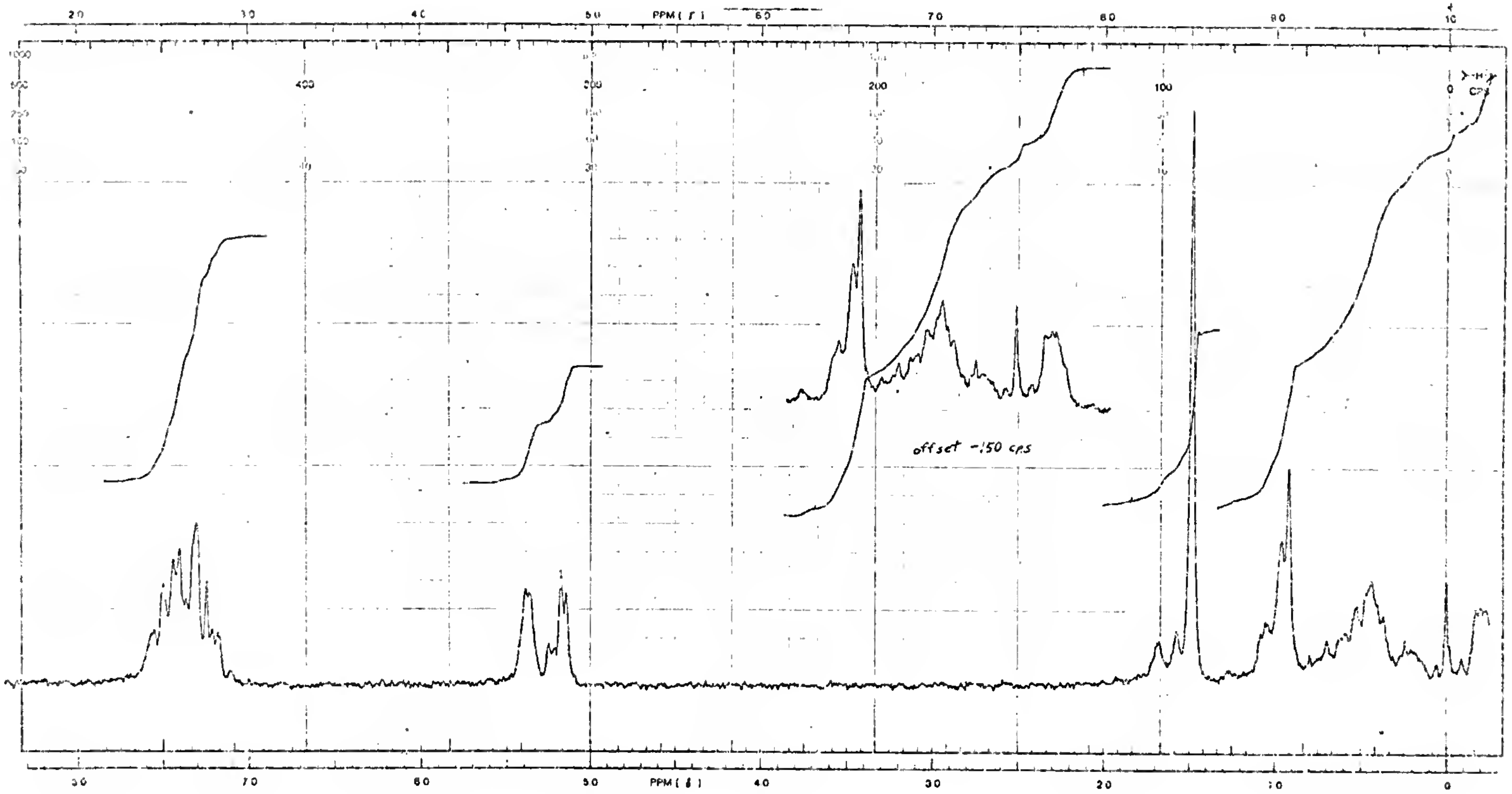


Figure A-5: Nmr of 7-cyclopropylcarbinyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38c)

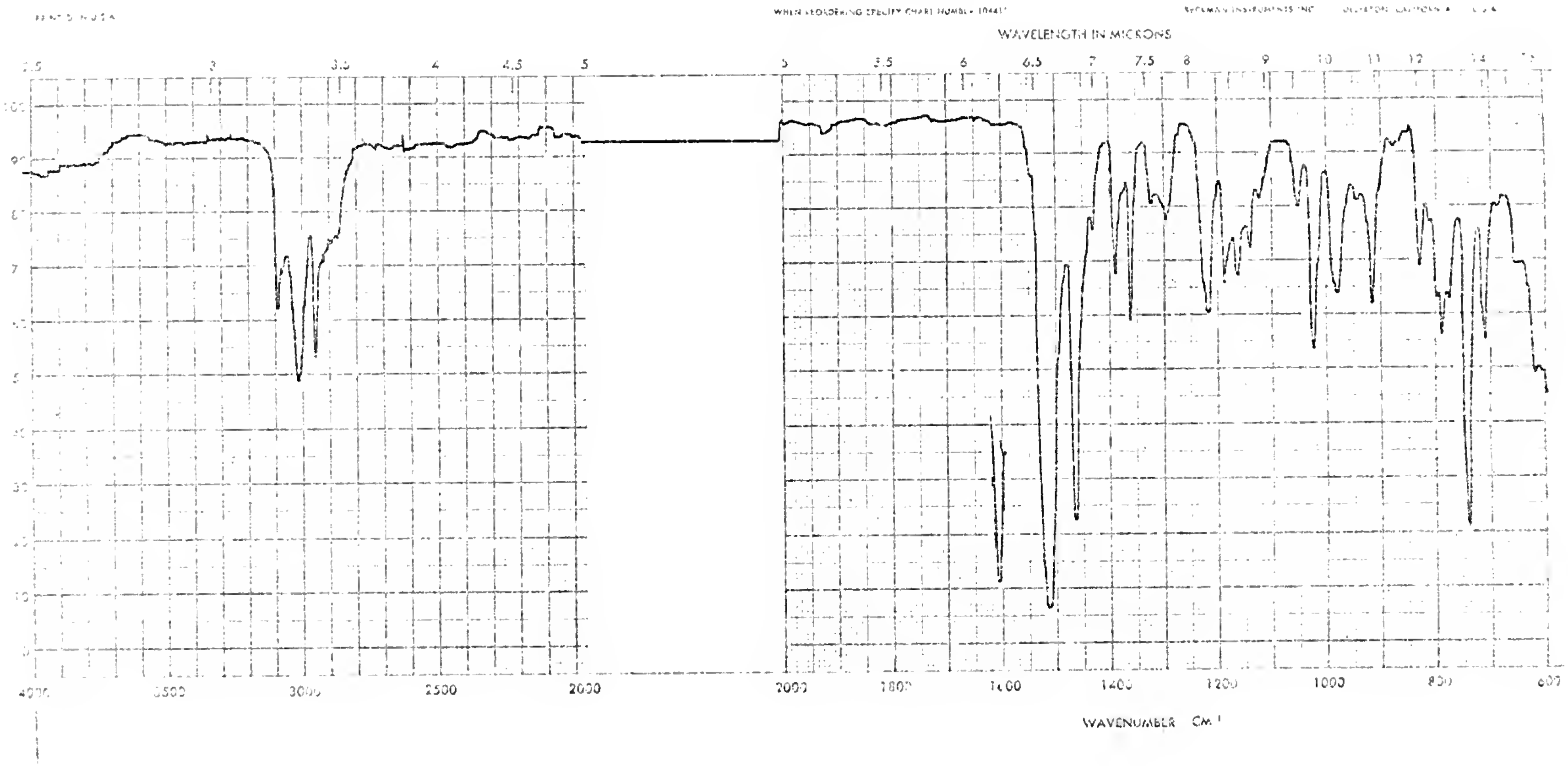


Figure A-6: Ir of 7-cyclopropylcarbinyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (<u>38c</u>)

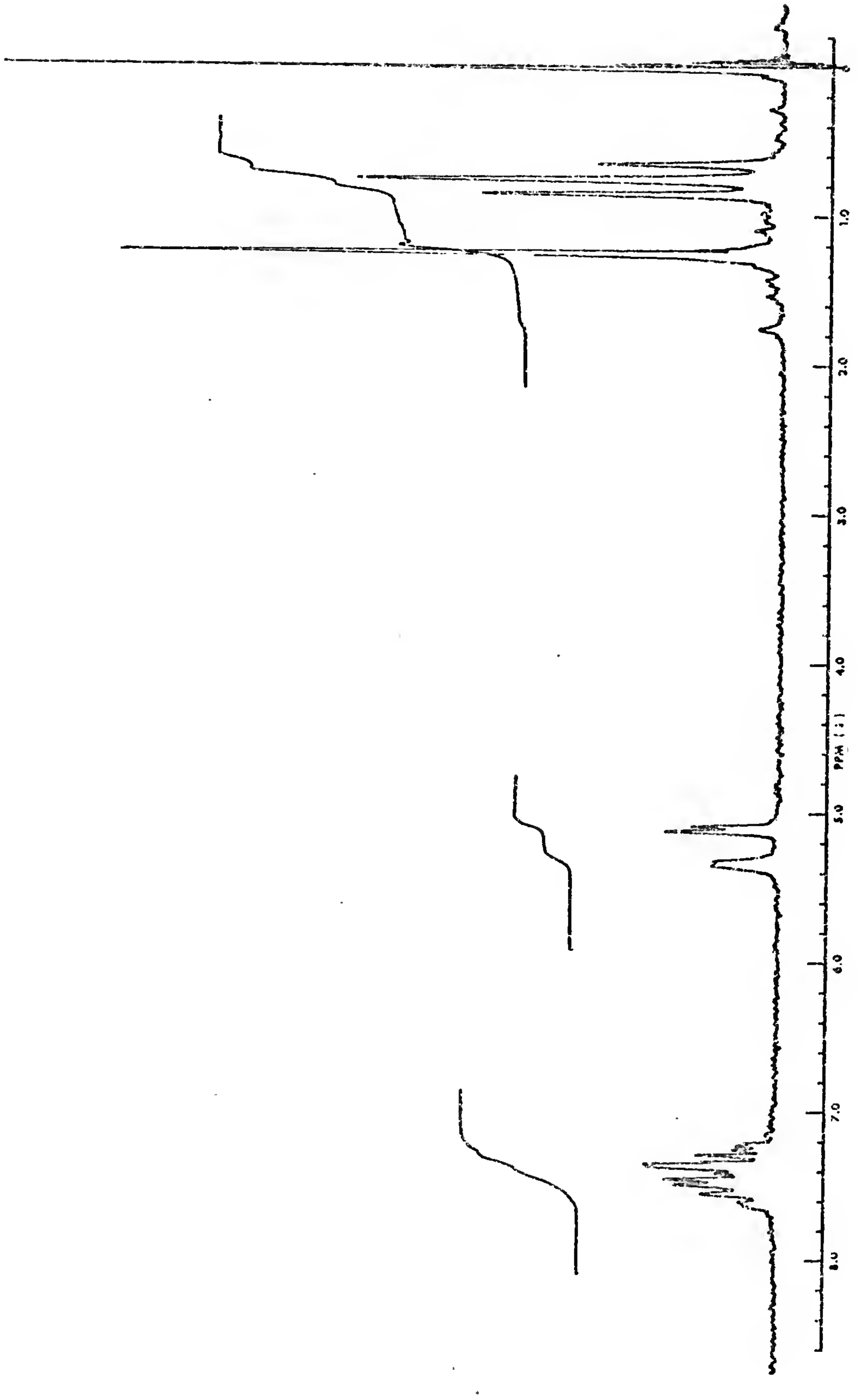


Figure A-7: Nmr of 7-isopropyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38d)

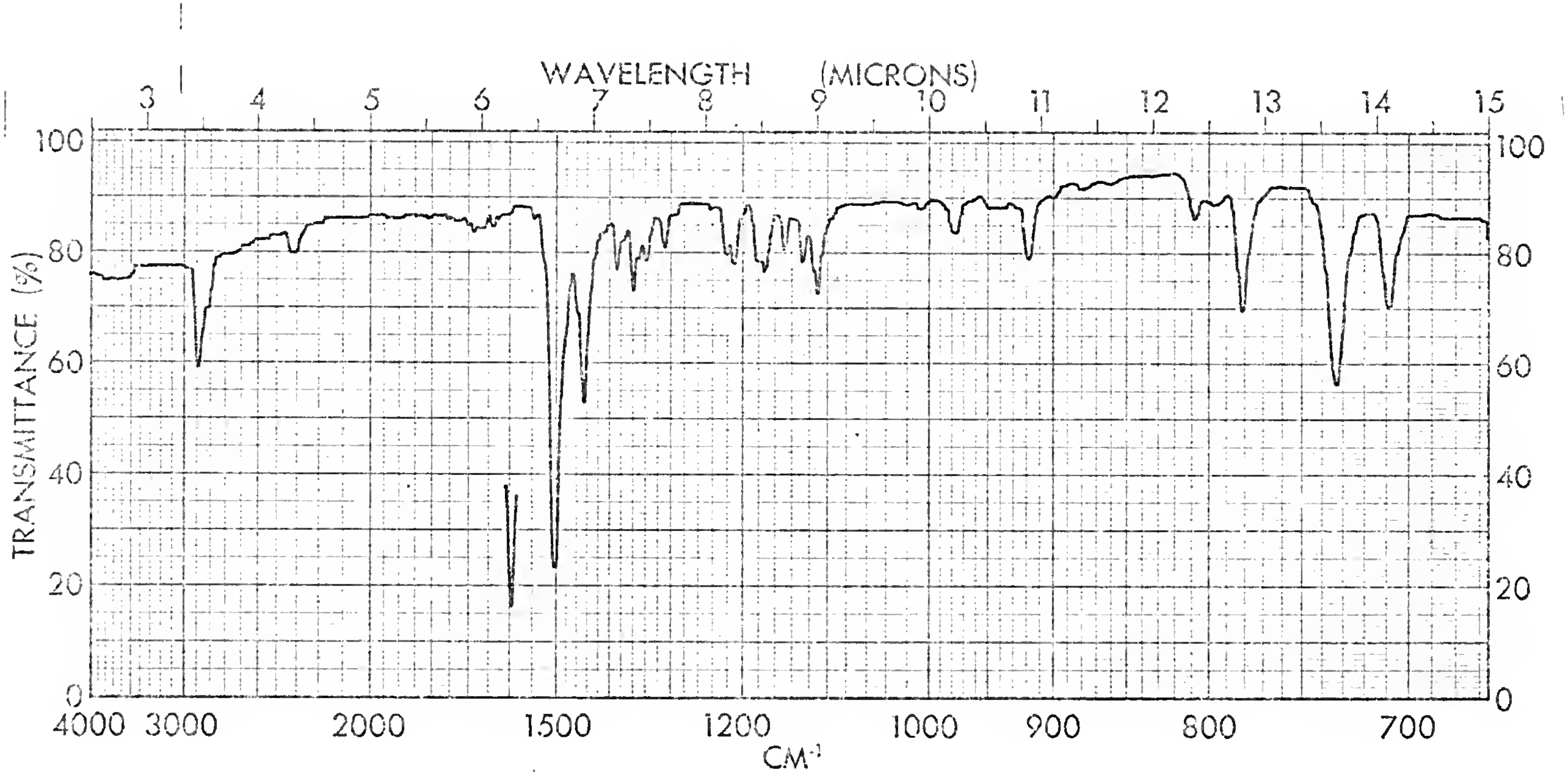


Figure A-8: Ir of 7-isopropyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38d)

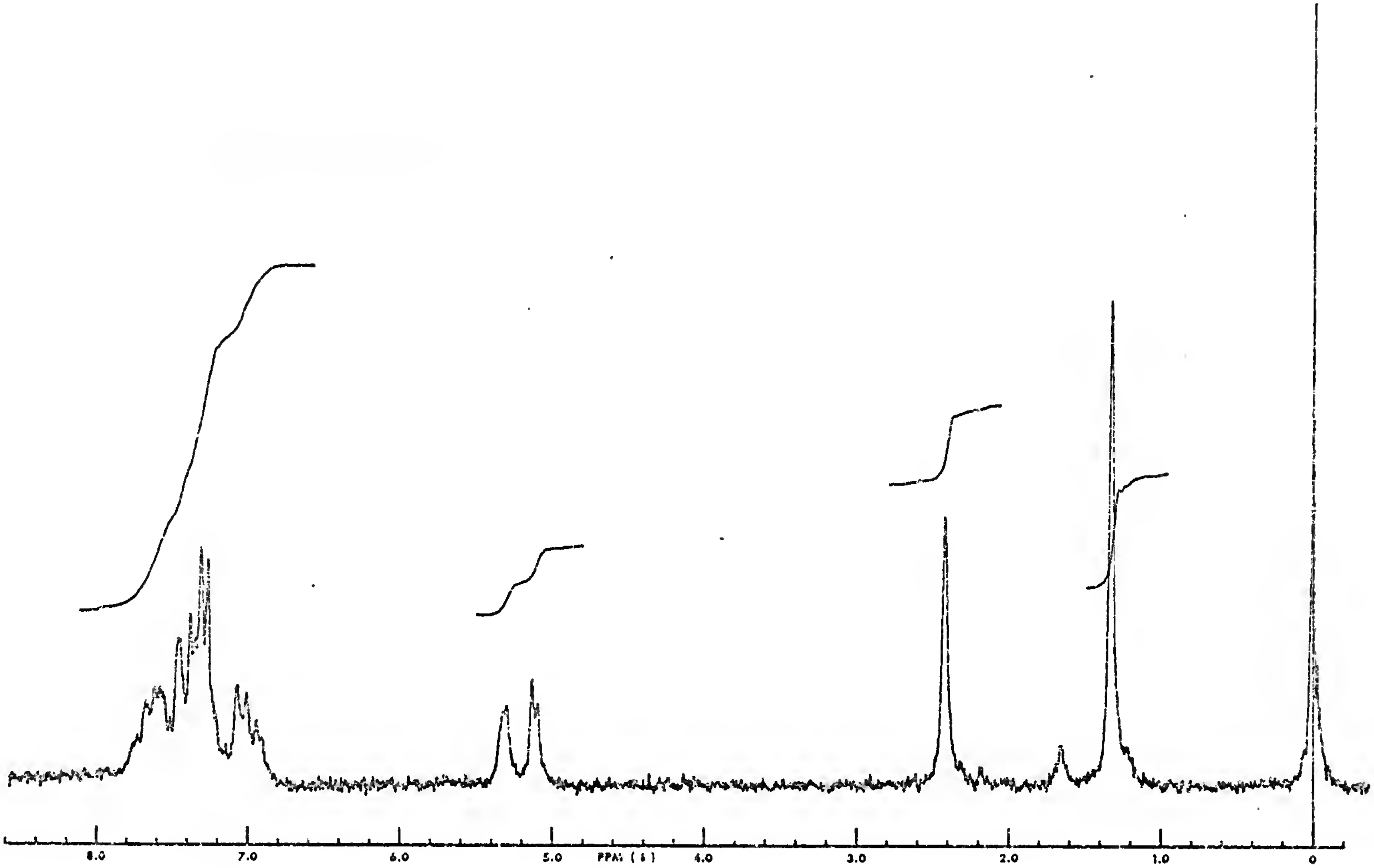


Figure A-9: Nmr of 7-benzyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38e)

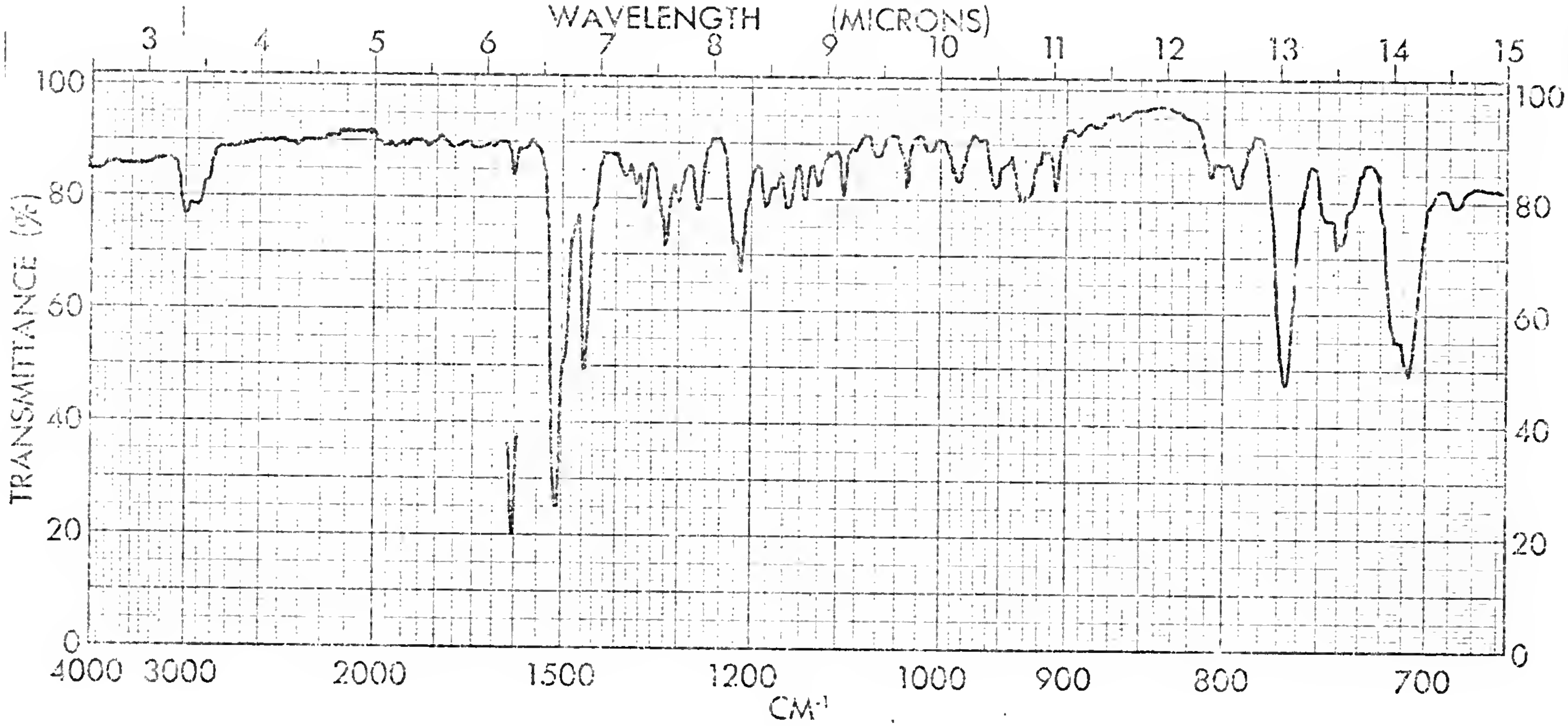


Figure A-10: Ir of 7-benzyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hepta-2,5-diene-5-N-oxide (38e)

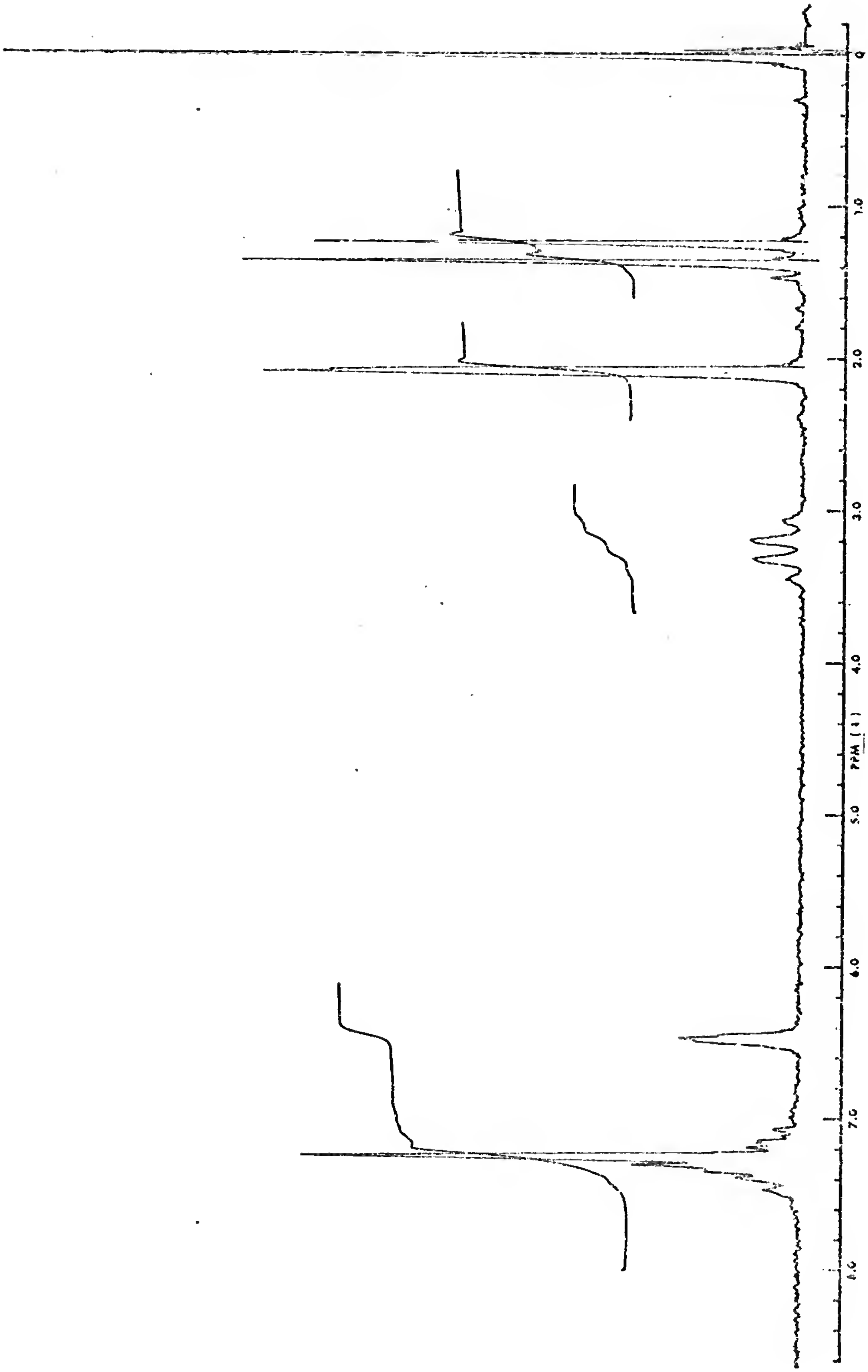


Figure A-11: Nmr of 1,2-dimethylindene (25)

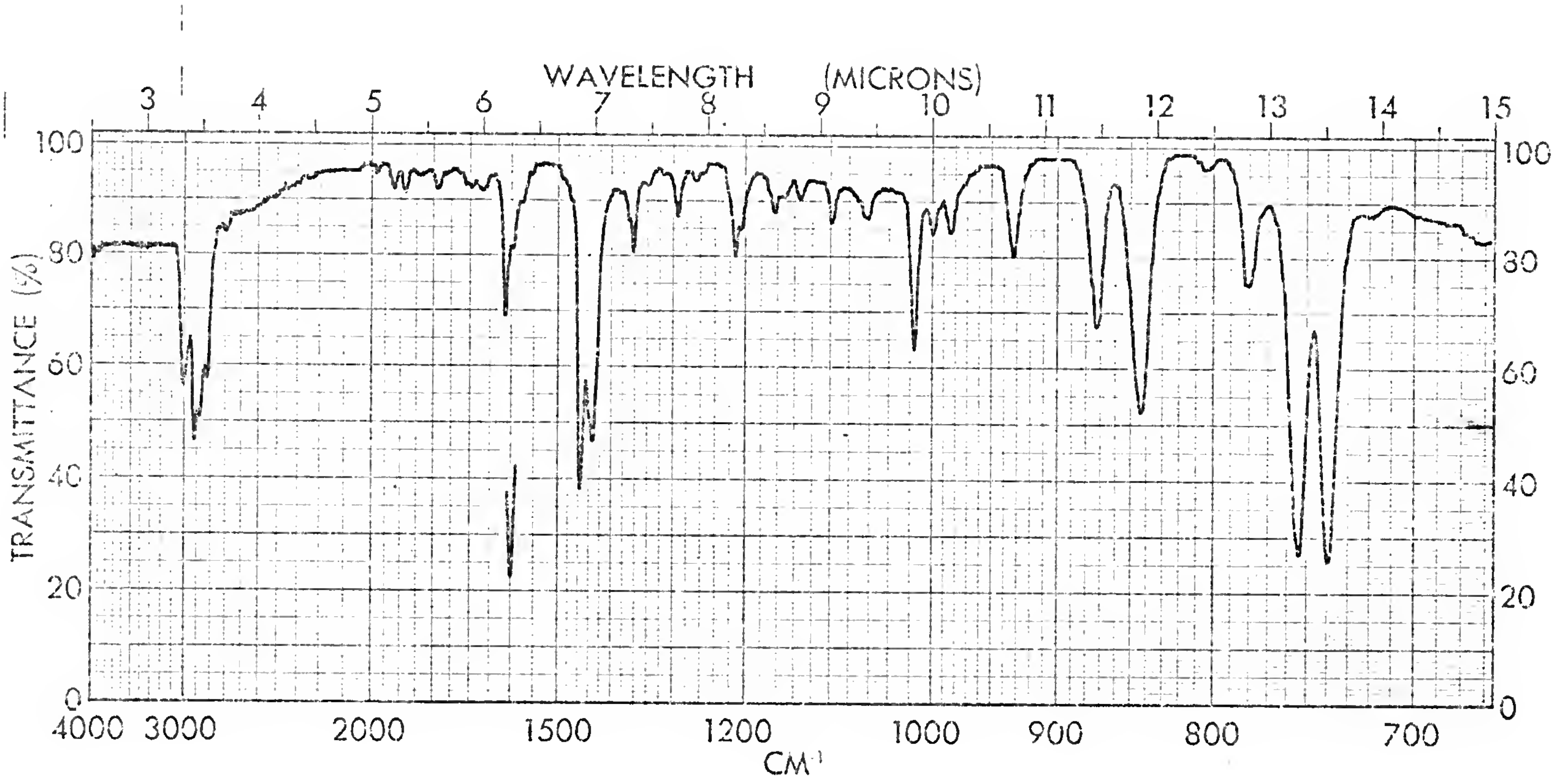


Figure A-12: Ir of 1,2-dimethylindene (<u>25</u>)

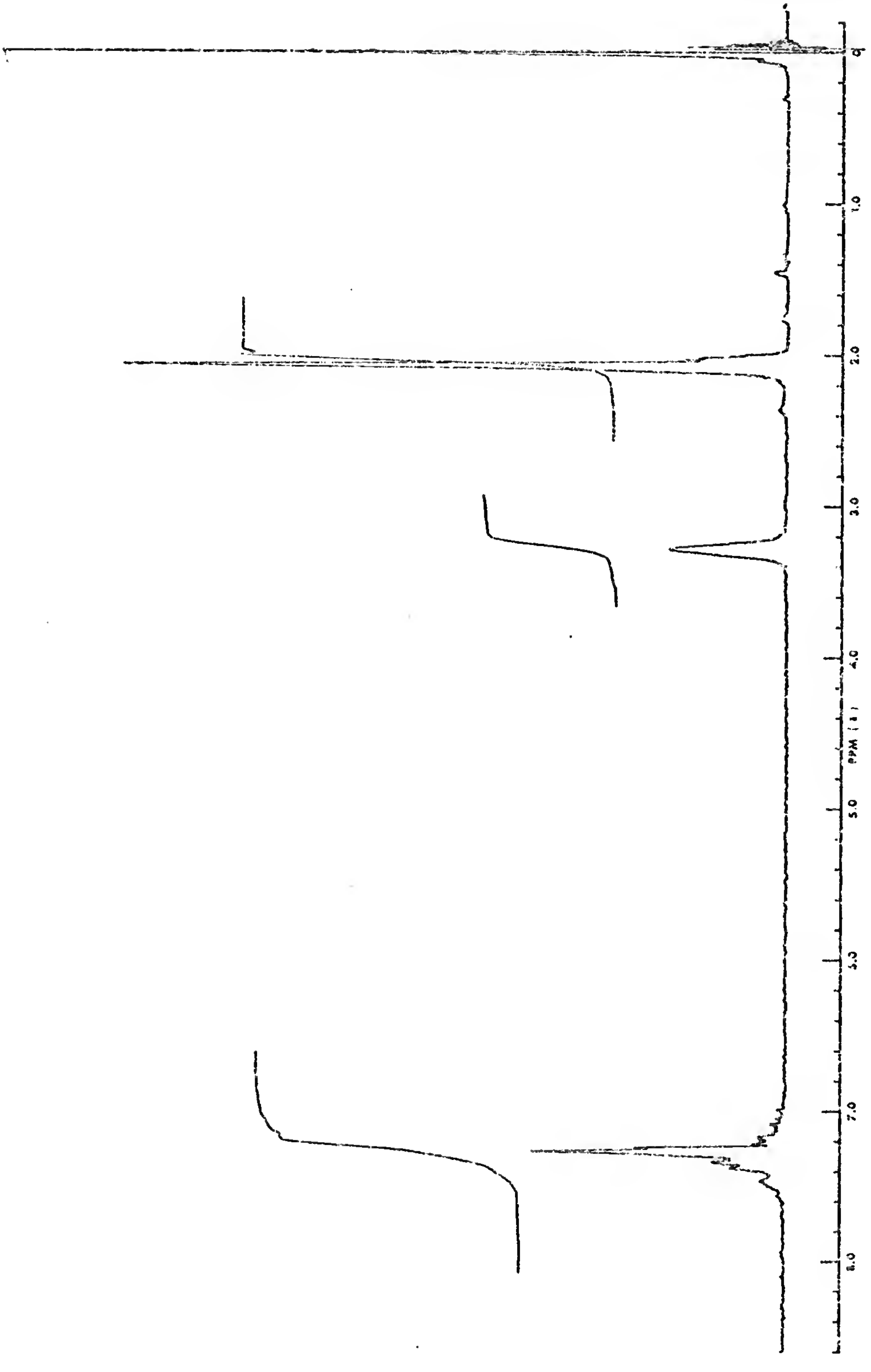


Figure A-13: Nmr of 2,3-dimethylindene (26)

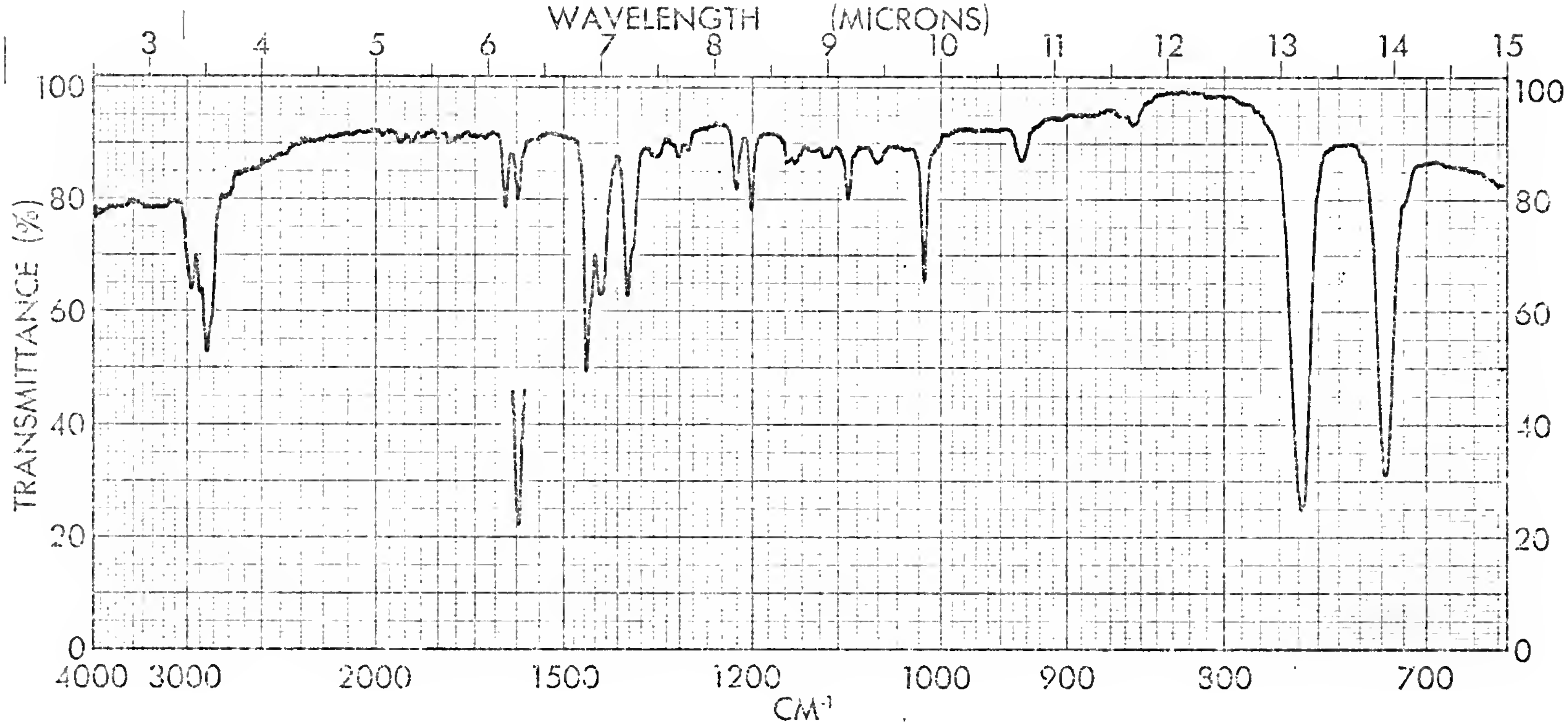


Figure A-14: Ir of 2,3-dimethylindene (26)

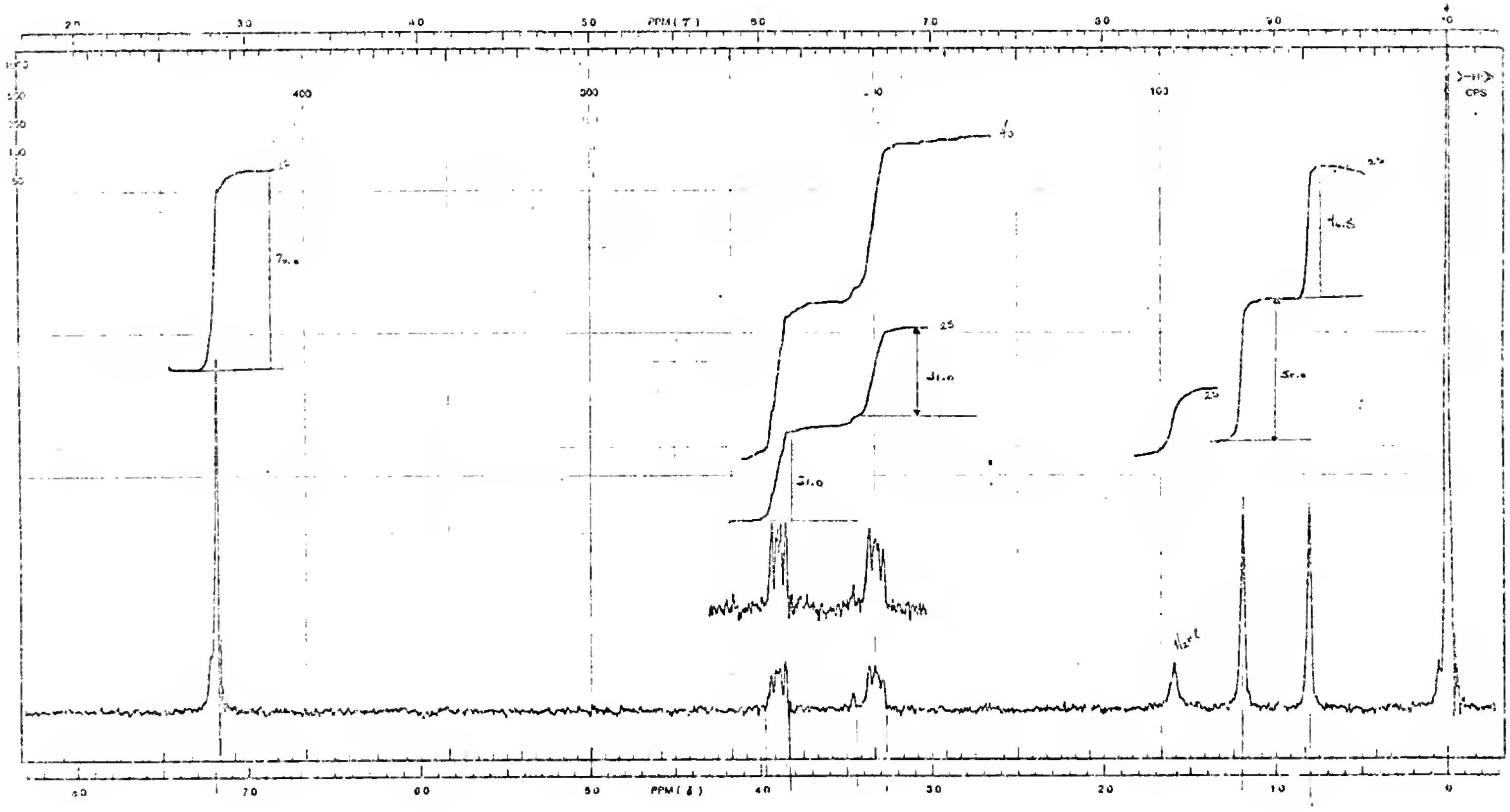


Figure A-15: Nmr of 1,4-dimethyl-1,4-endomethylene-tetralin-2,3-dicarboxylic anhydride (28b)

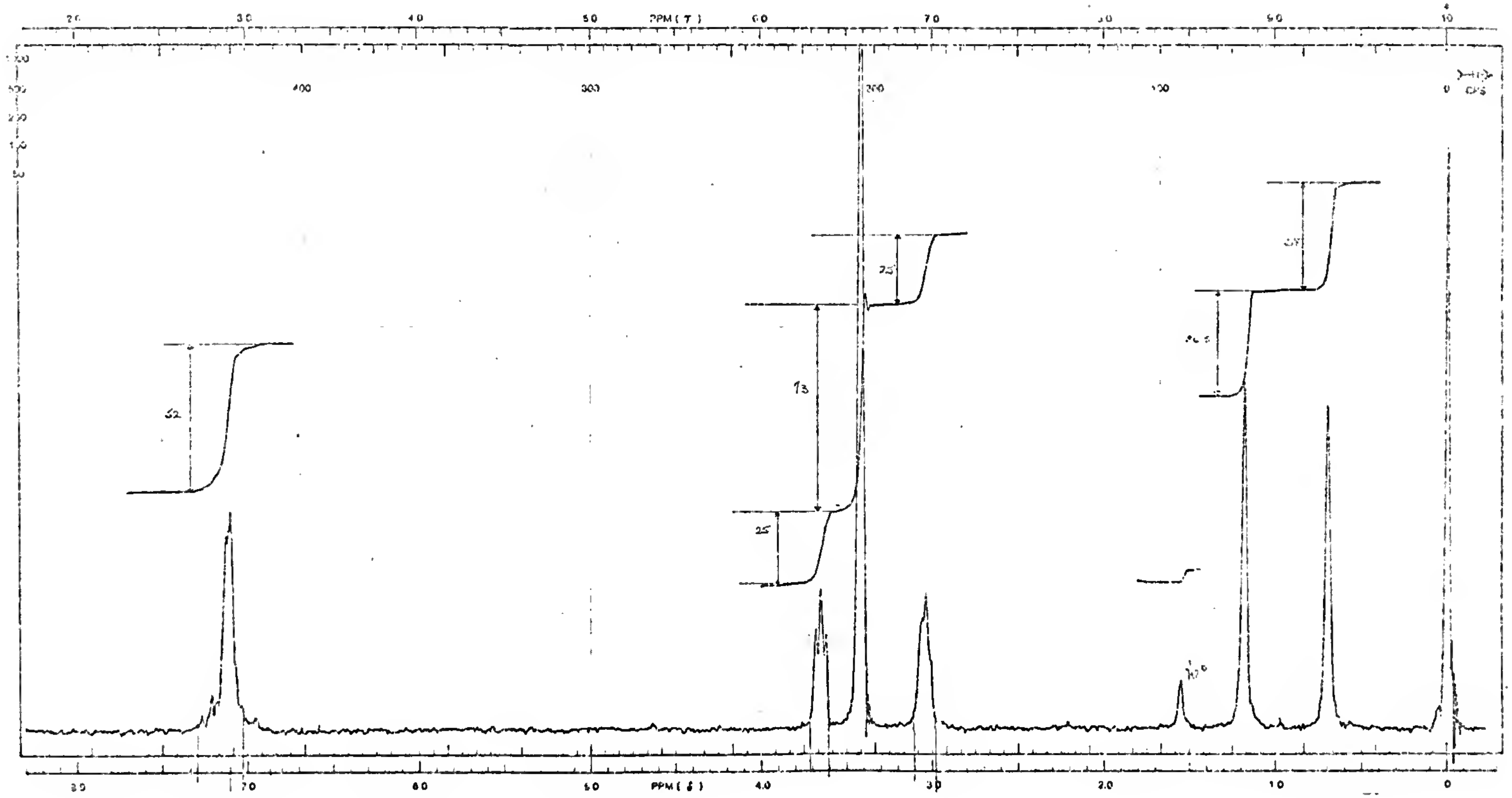


Figure A-16: Nmr of dimethyl endo, cis-7,7-dimethyl-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (54)

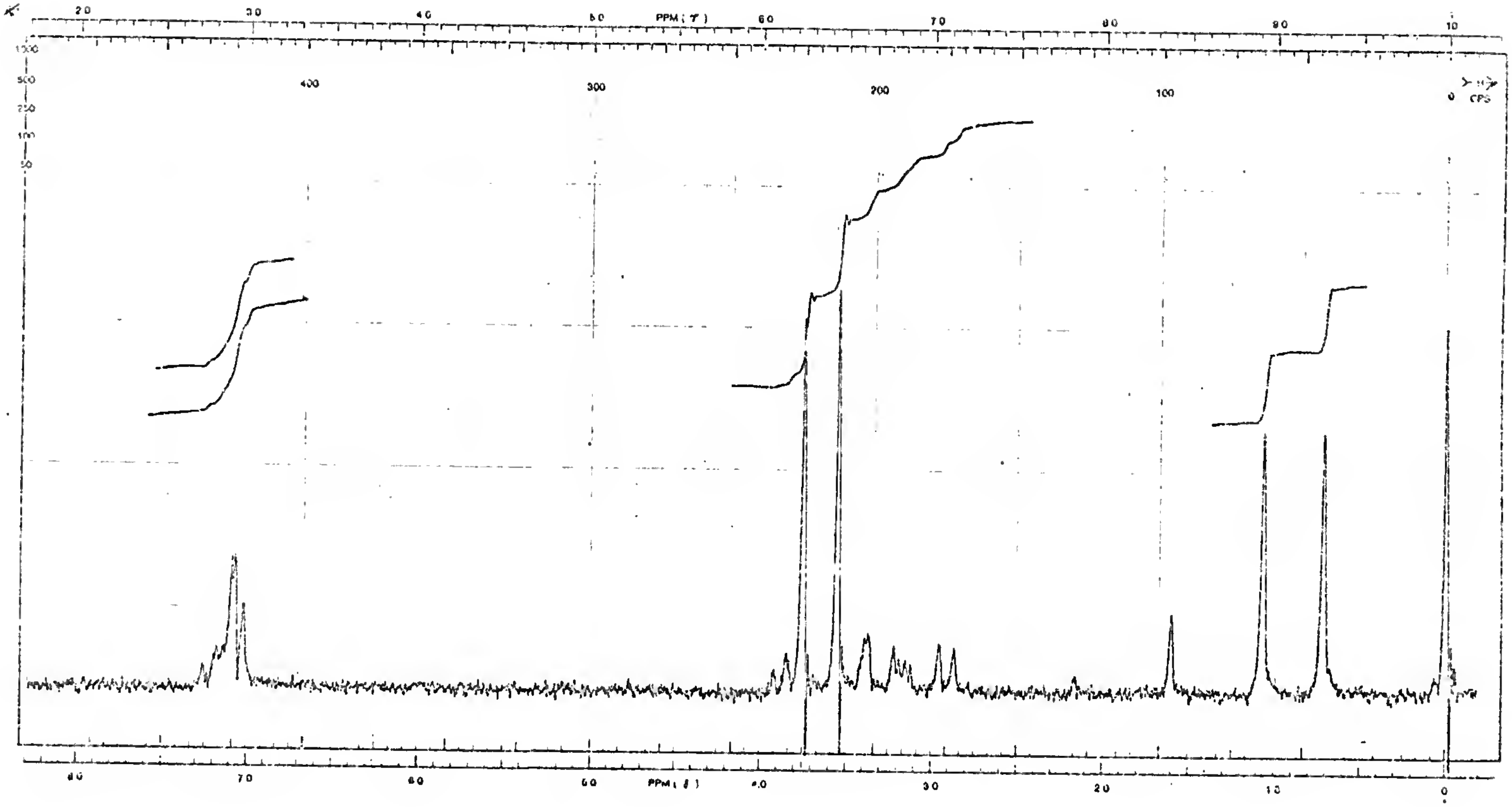


Figure A-17: Nmr of dimethyl trans-7,7-dimethyl-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (55)

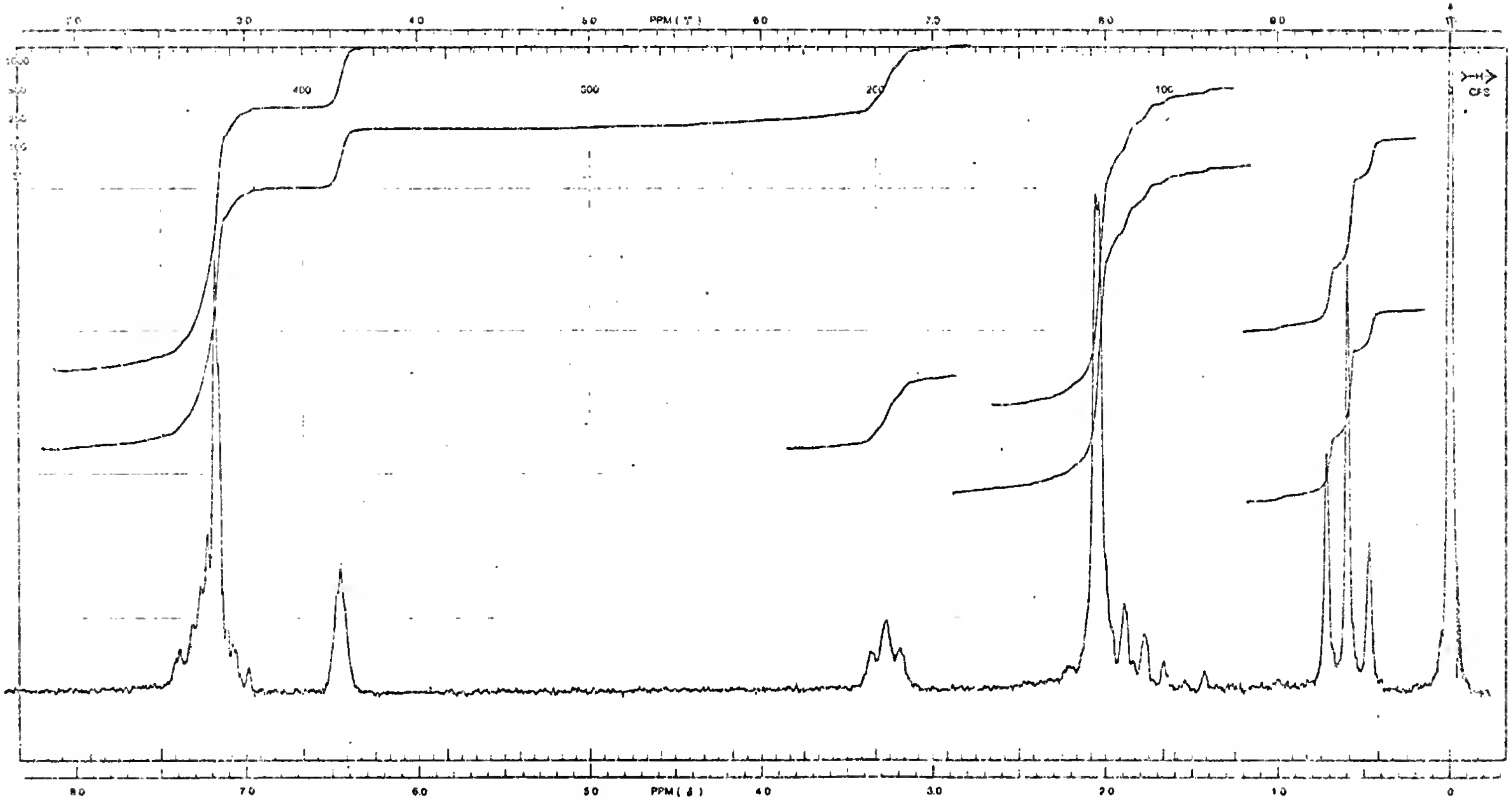


Figure A-18: Nmr of 1-ethyl-2-methylindene (56a)

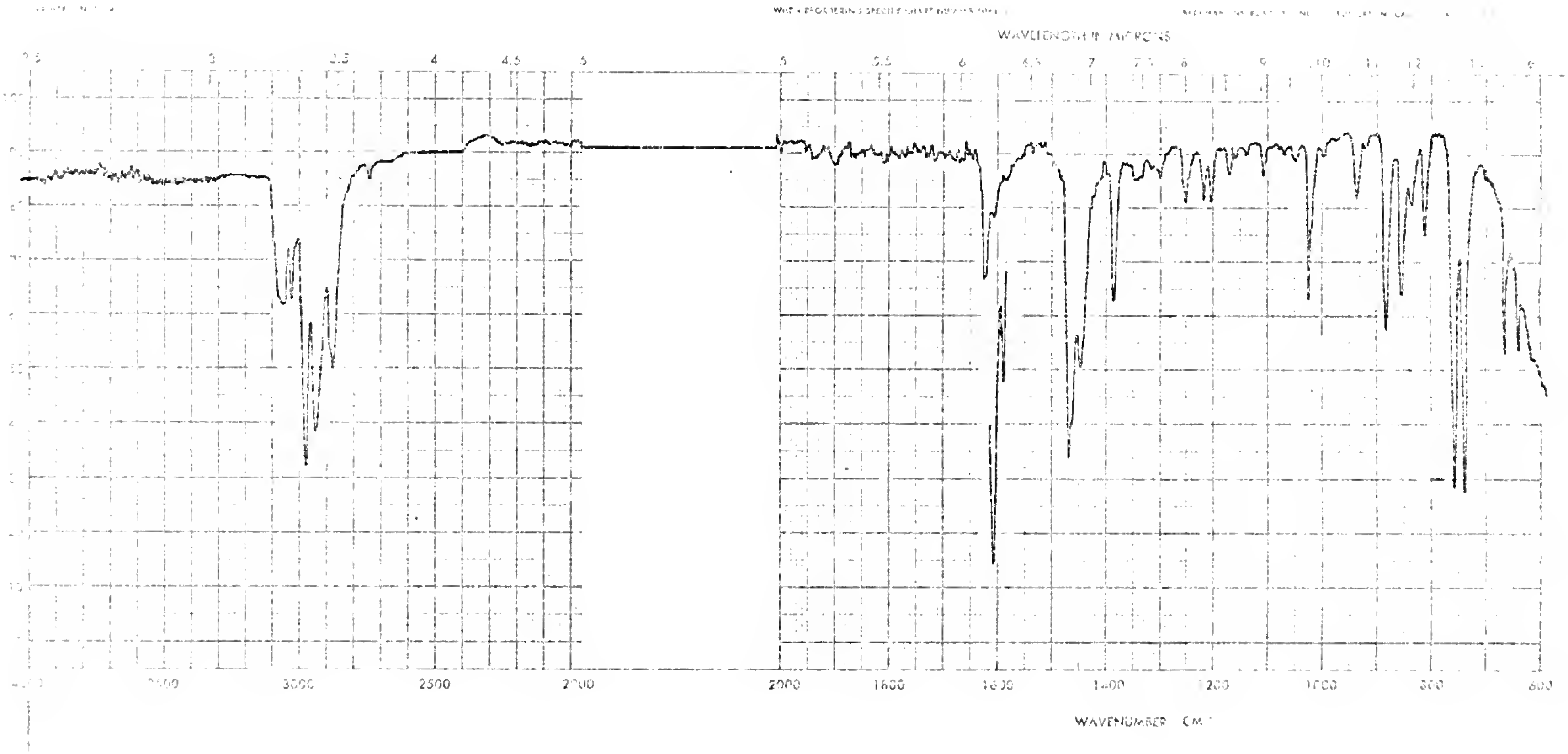


Figure A-19: Ir of 1-ethyl-2-methylindene (56a)

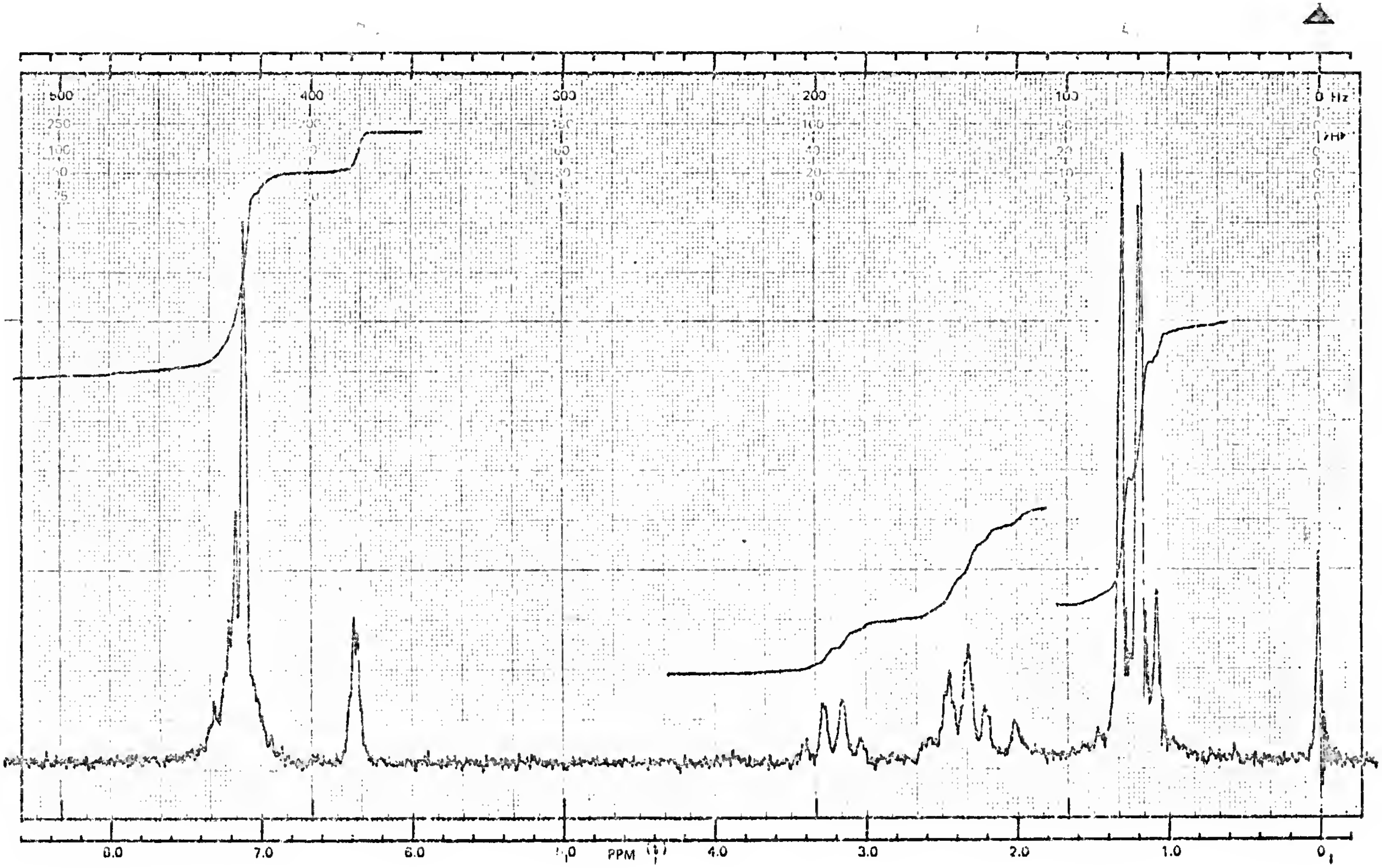


Figure A-20: Nmr of 1-methyl-2-ethylindene (56b)

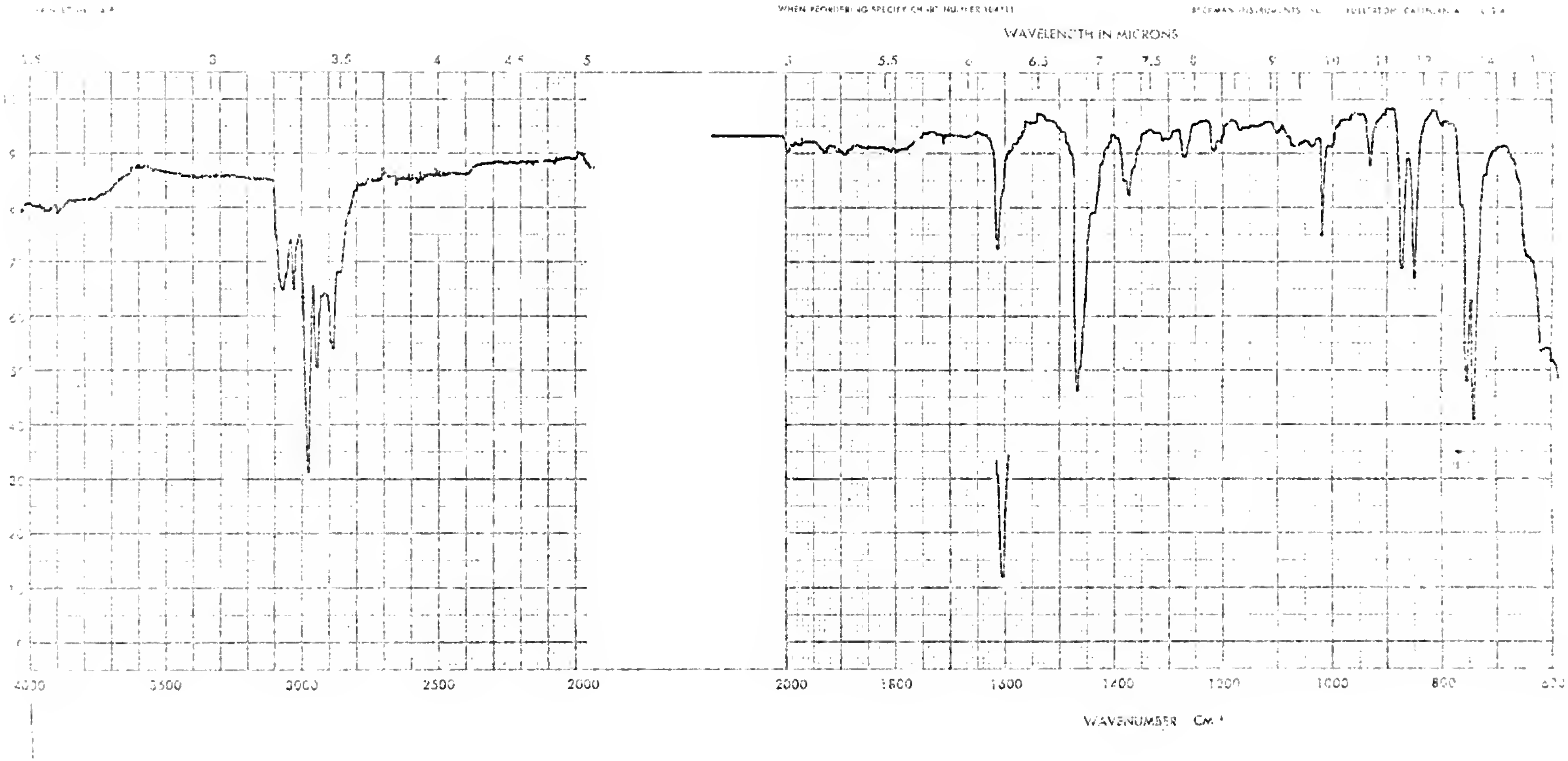


Figure A-21: Ir of 1-methyl-2-ethylindene (56b)

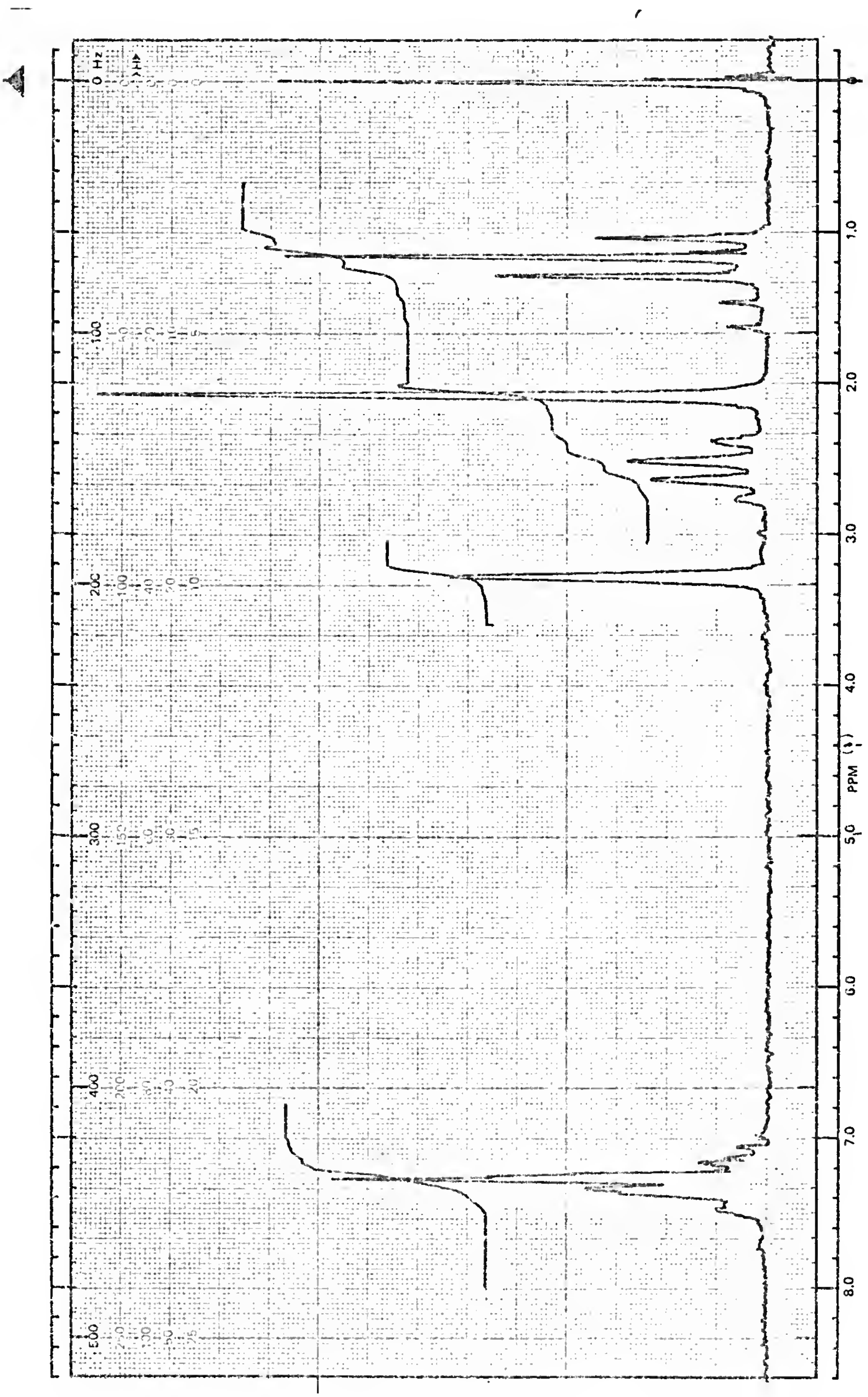


Figure A-22: Nmr of 2-methyl-3-ethylindene (56c)

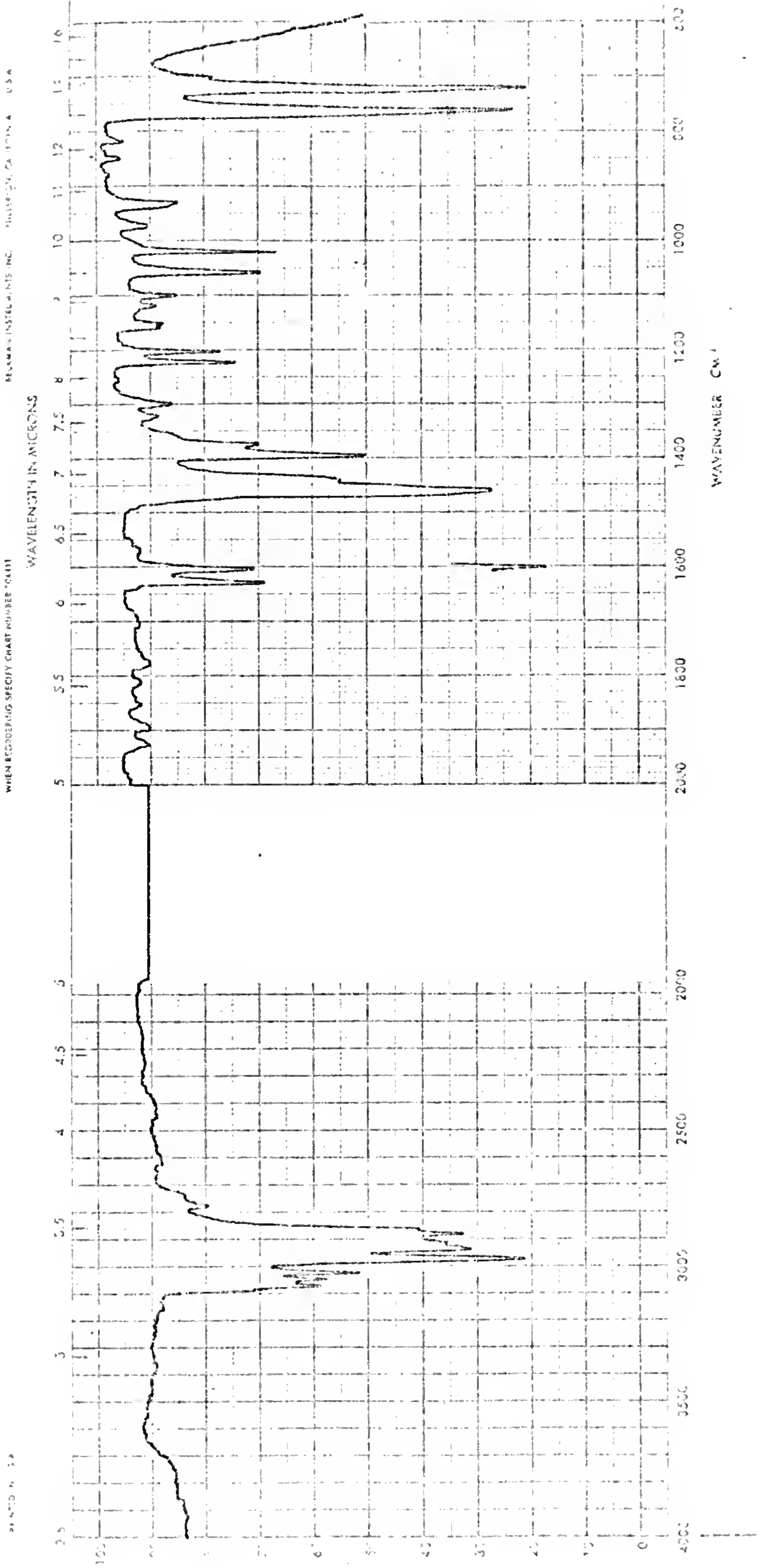


Figure A-23: Ir of 2-methyl-3-ethylindene (56c)

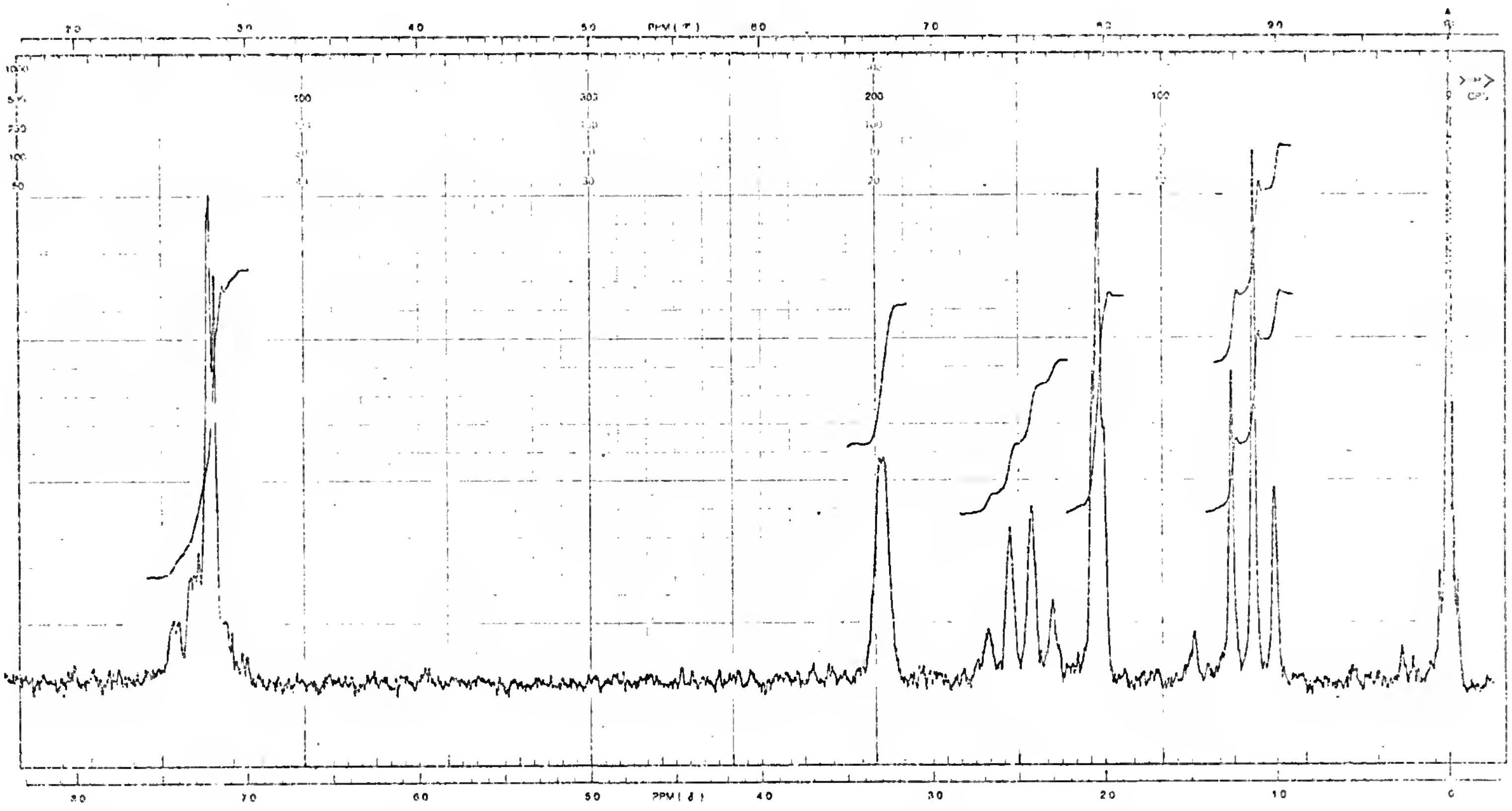


Figure A-24: Nmr of 2-ethyl-3-methylindene (<u>56d</u>)

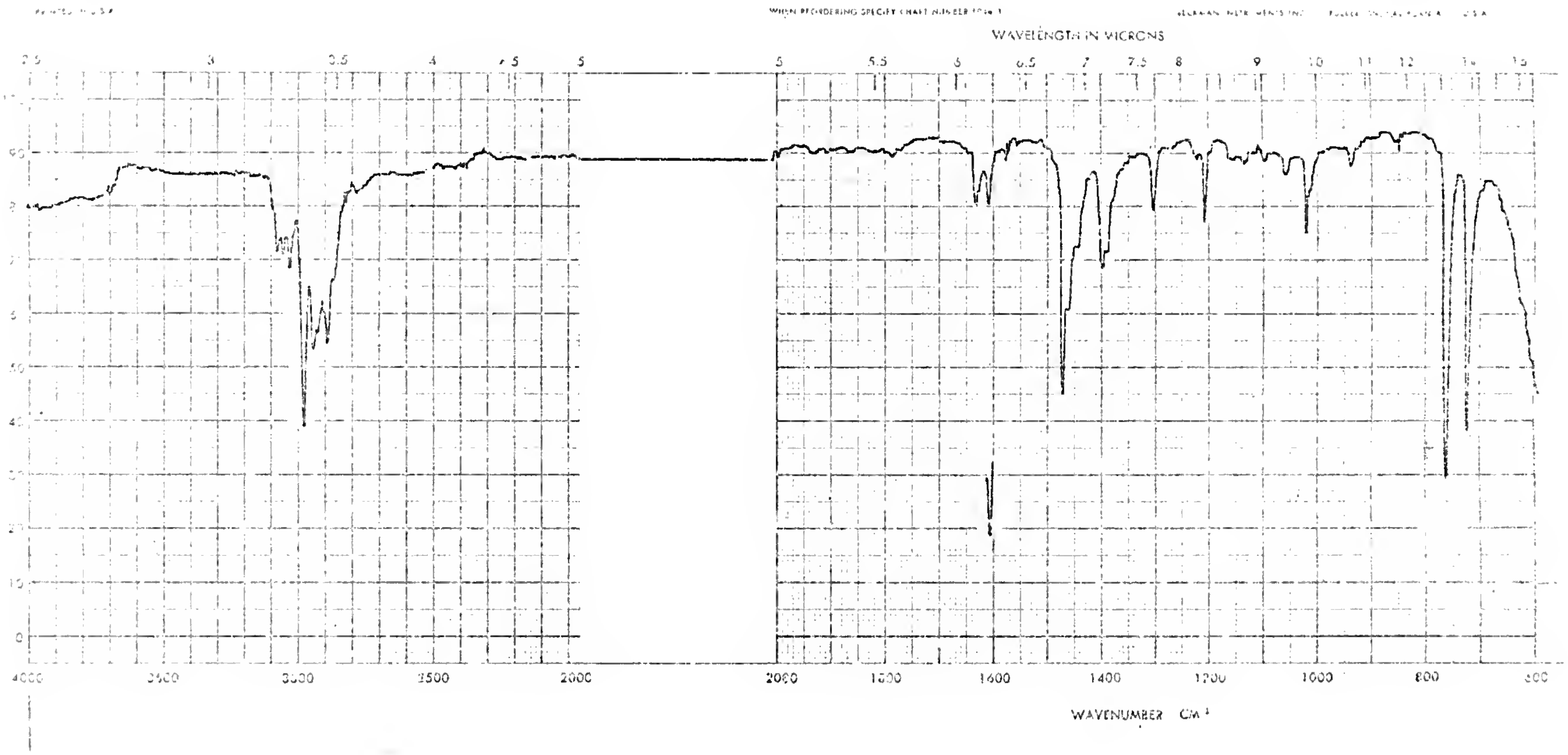


Figure A-25: Ir of 2-ethyl-3-methylindene (<u>56d</u>)

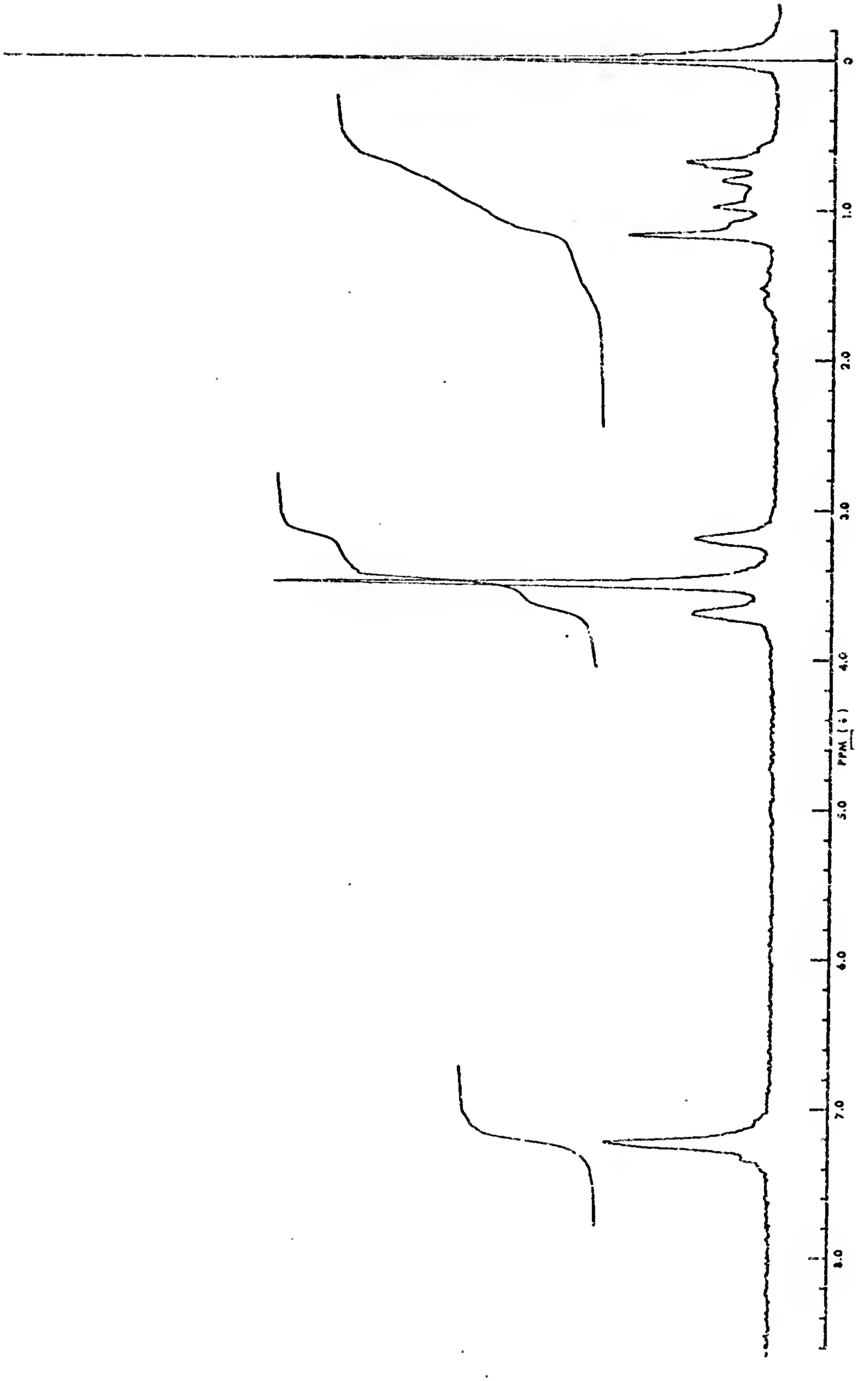


Figure A-26: Nmr of dimethyl endo, cis-7-ethyl-7-methyl-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (57)

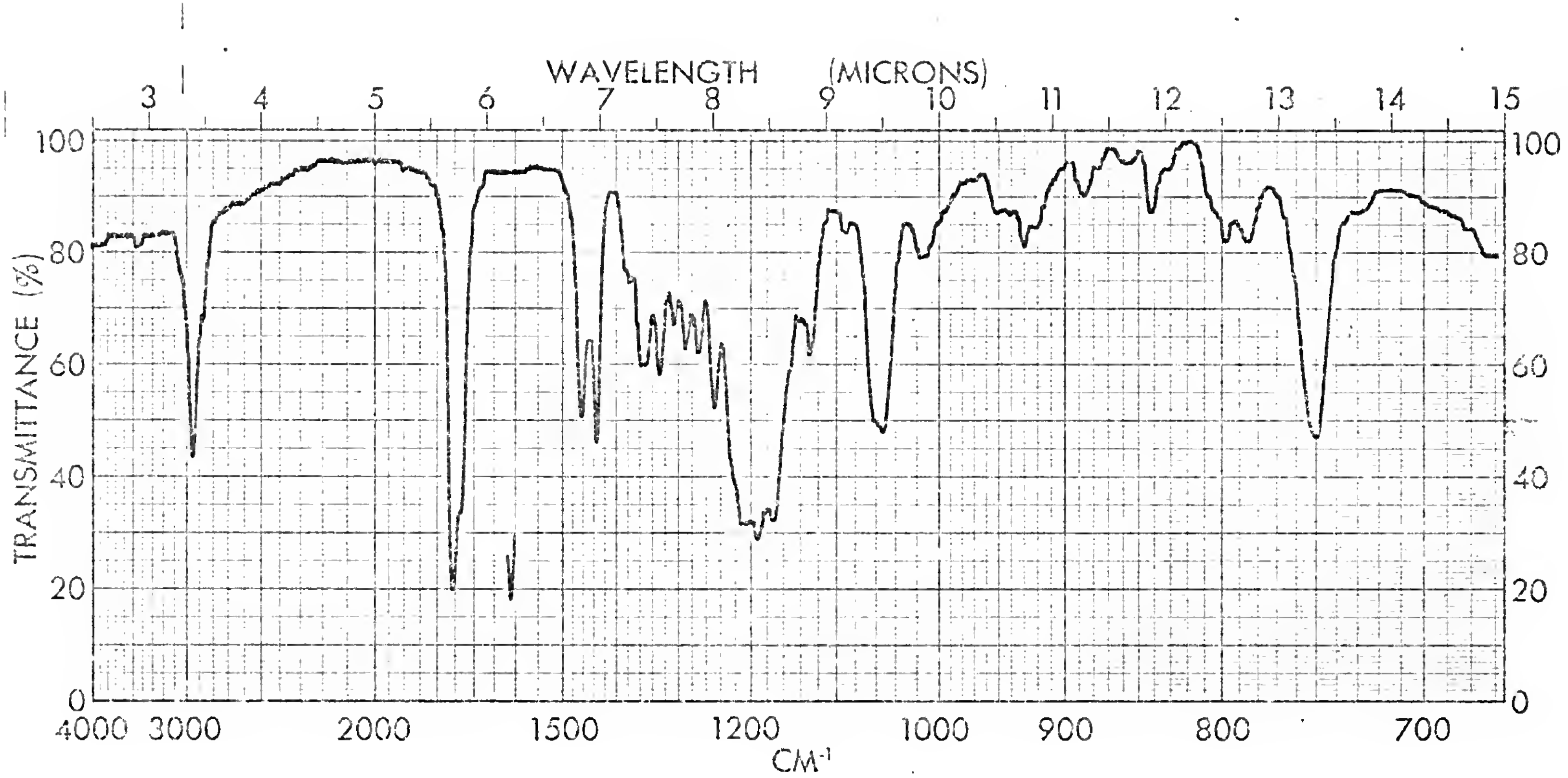


Figure A-27: Ir of dimethyl endo, cis-7-ethyl-7-methyl-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (<u>57</u>)

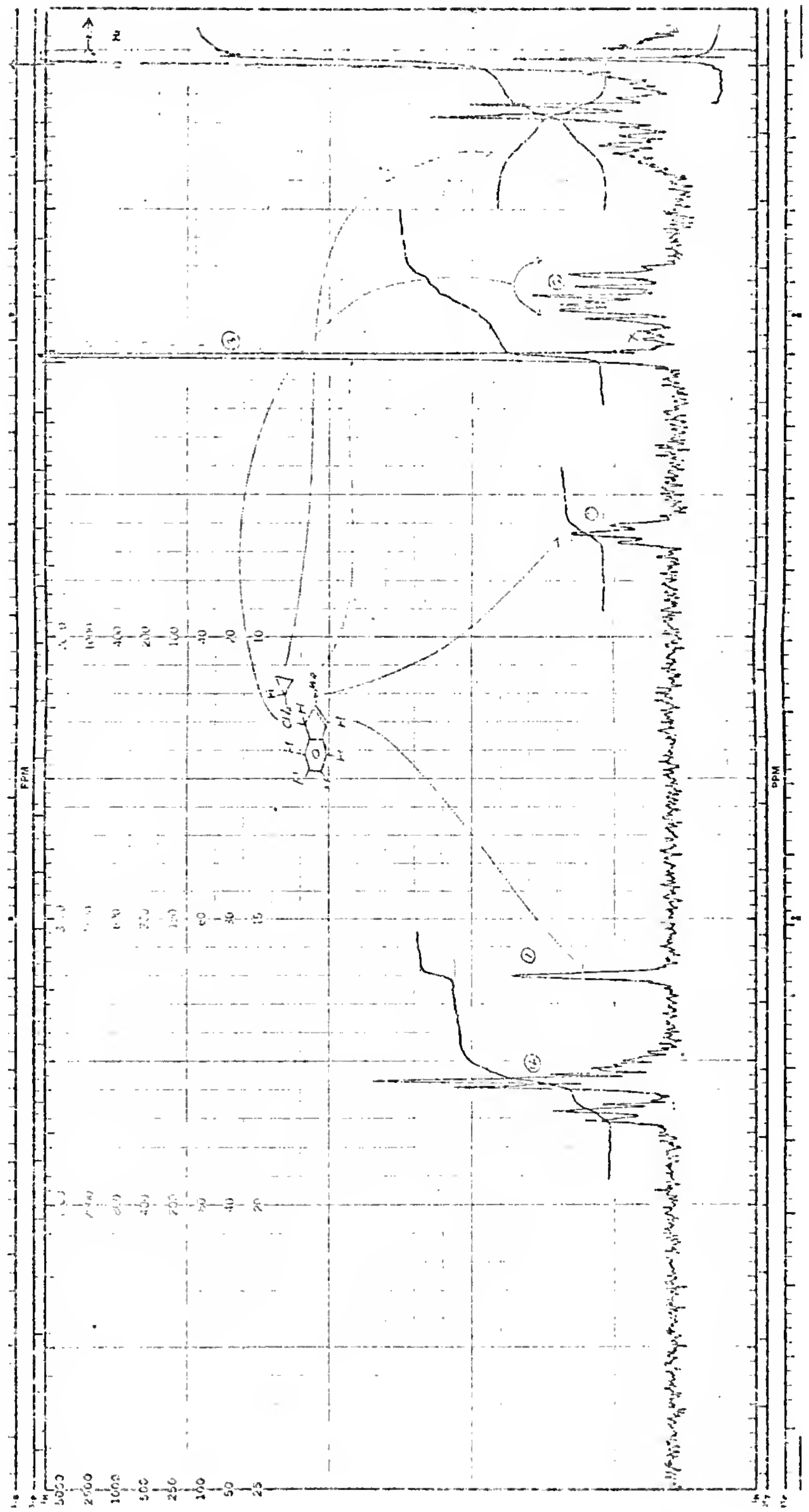


Figure A-28: 100 MHz ^{1}H nmr of 1-cyclopropylcarbinyl-2-methylindene (<u>58a</u>)

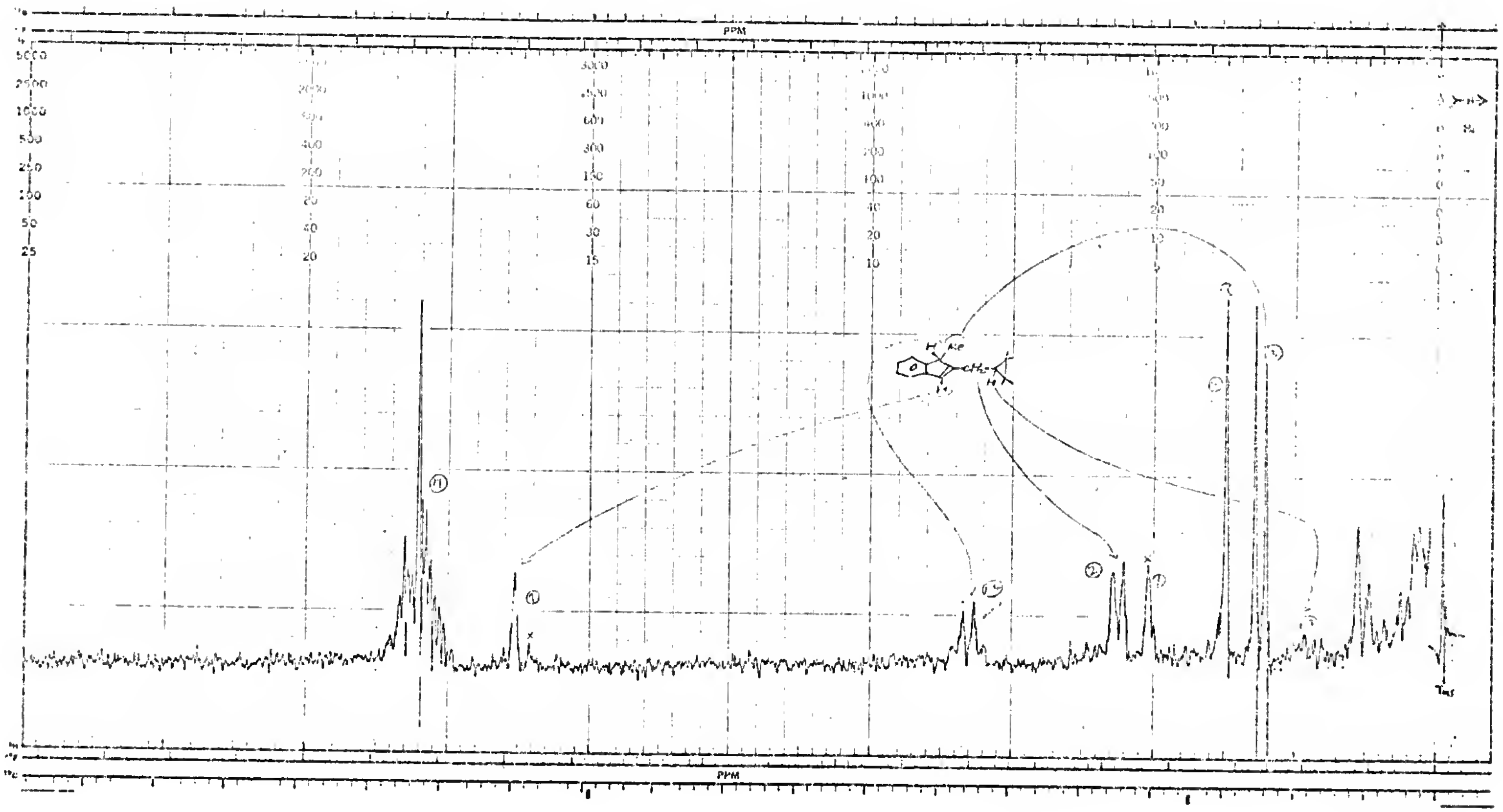


Figure A-29: 100 MHz ^{1}H nmr of 1-methyl-2-cyclopropylcarbinylindene (58b)

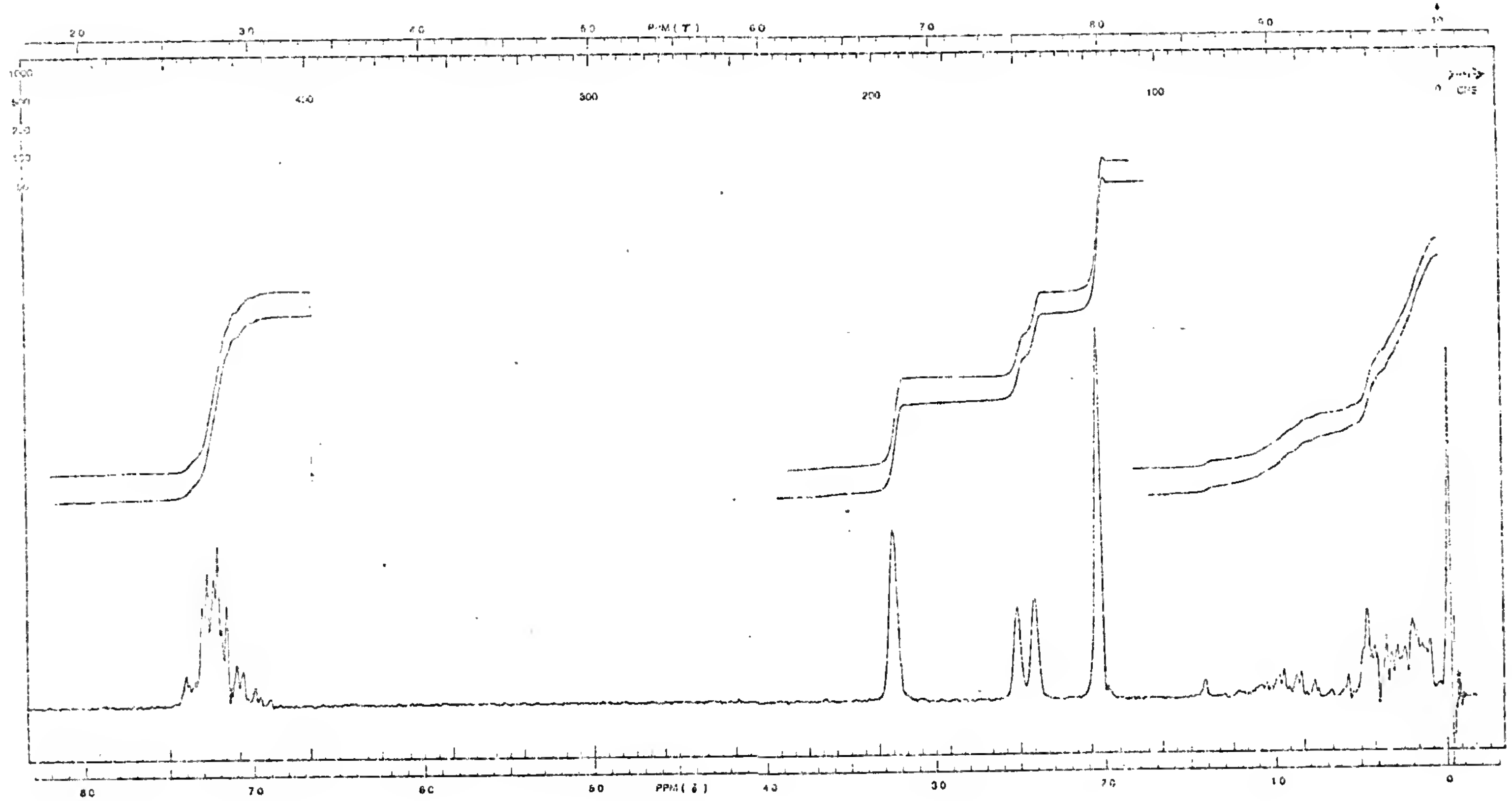


Figure A-30: Nmr of 2-methyl-3-cyclopropylcarbinylindene (<u>58c</u>)

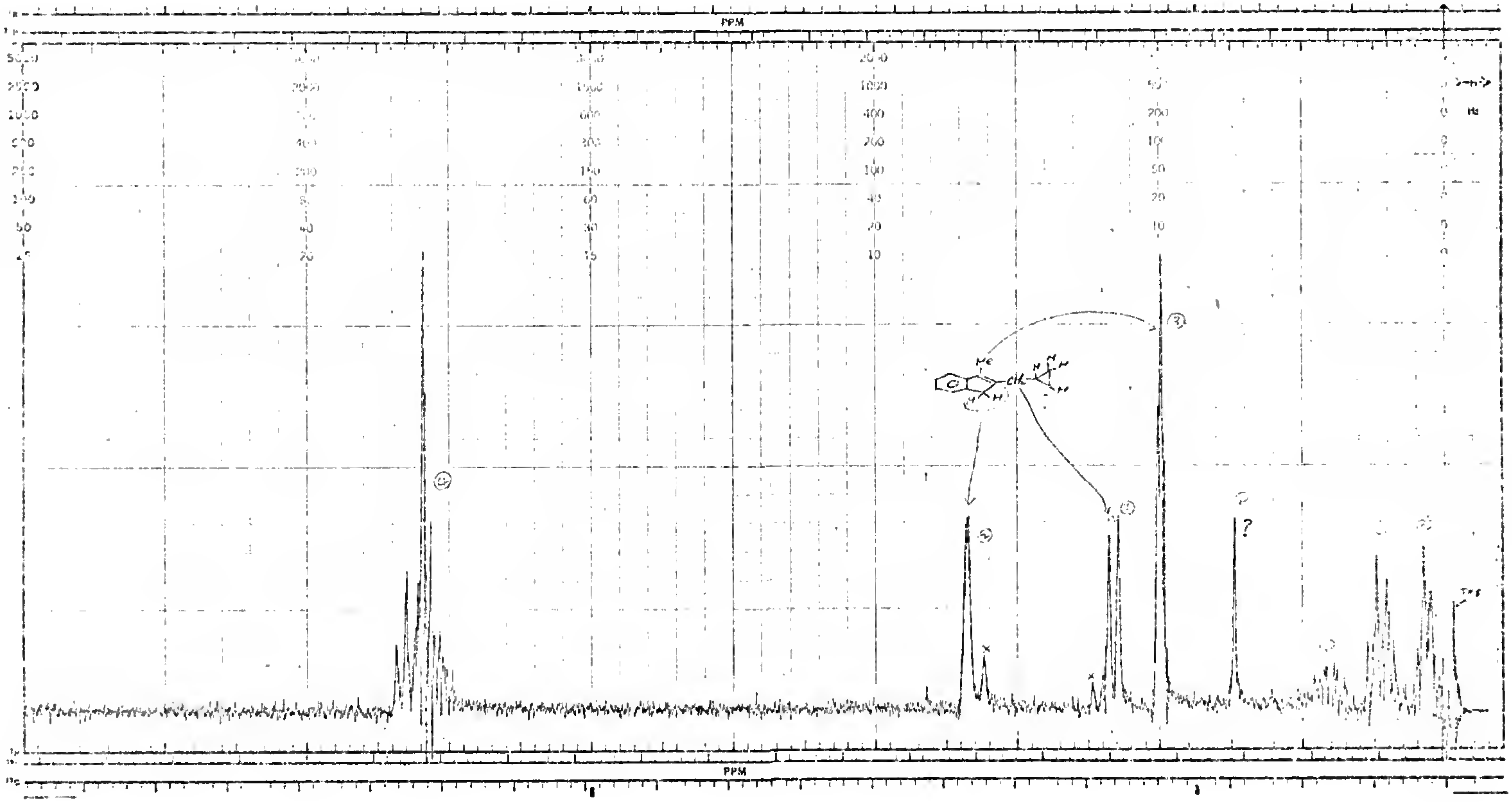


Figure A-31: 100 MHz ^{1}H nmr of 2-cyclopropylcarbinyl-3-methylindene (58d)

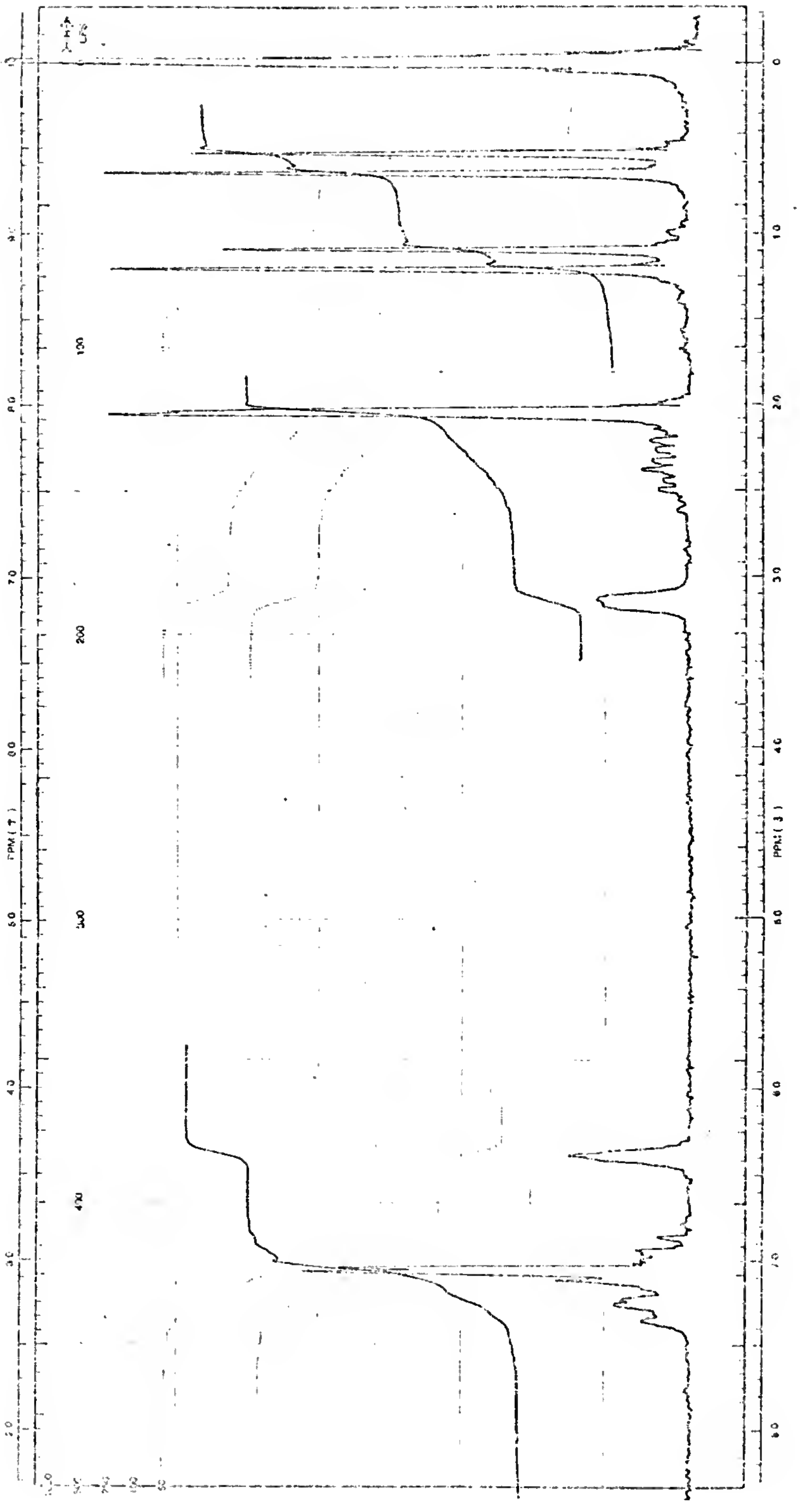


Figure A-32: Nmr of 1-isopropyl-2-methylindene (63a)

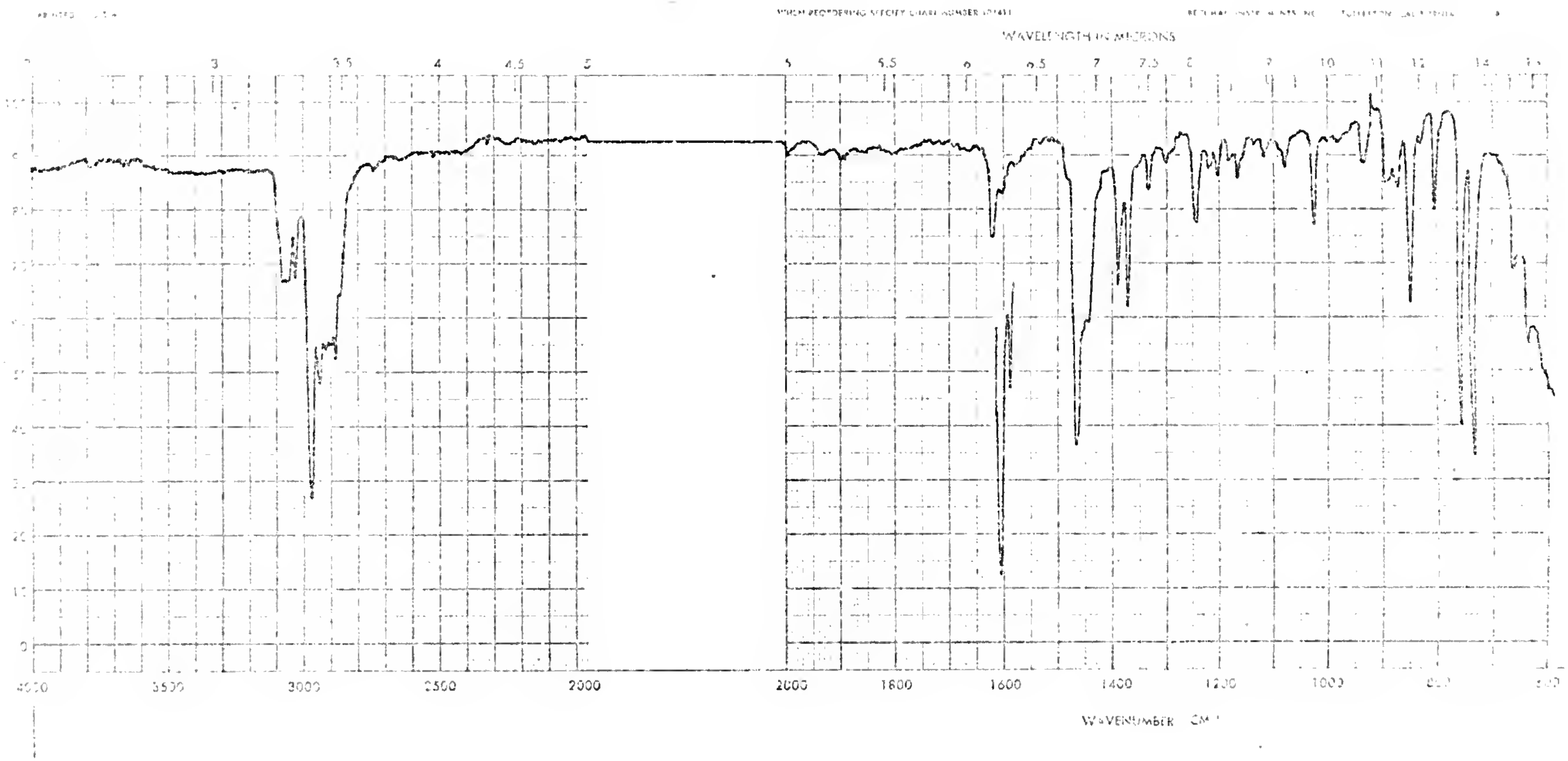


Figure A-33: Ir of 1-isopropyl-2-methylindene (63a)

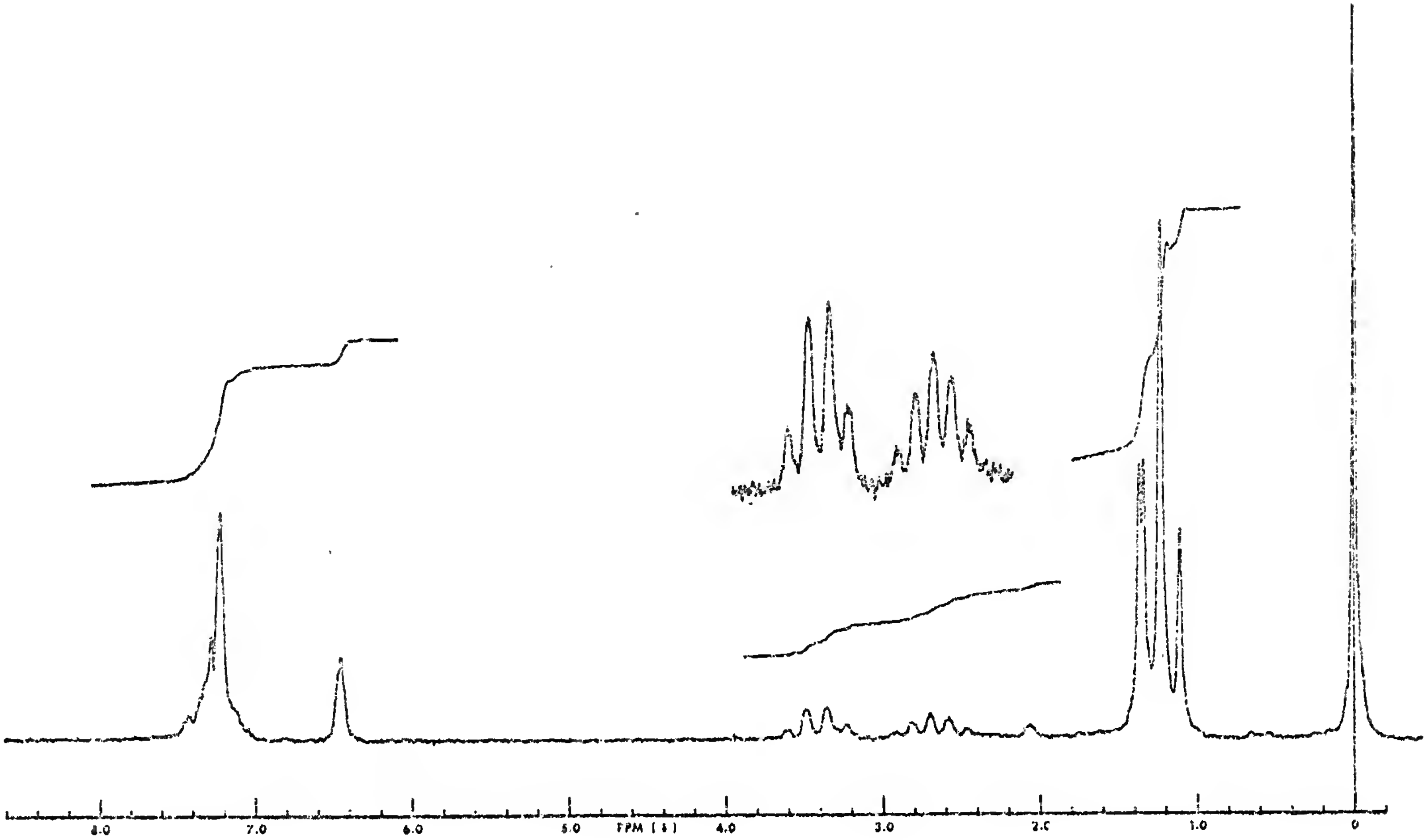


Figure A-34: Nmr of 1-methyl-2-isopropylindene (63b)

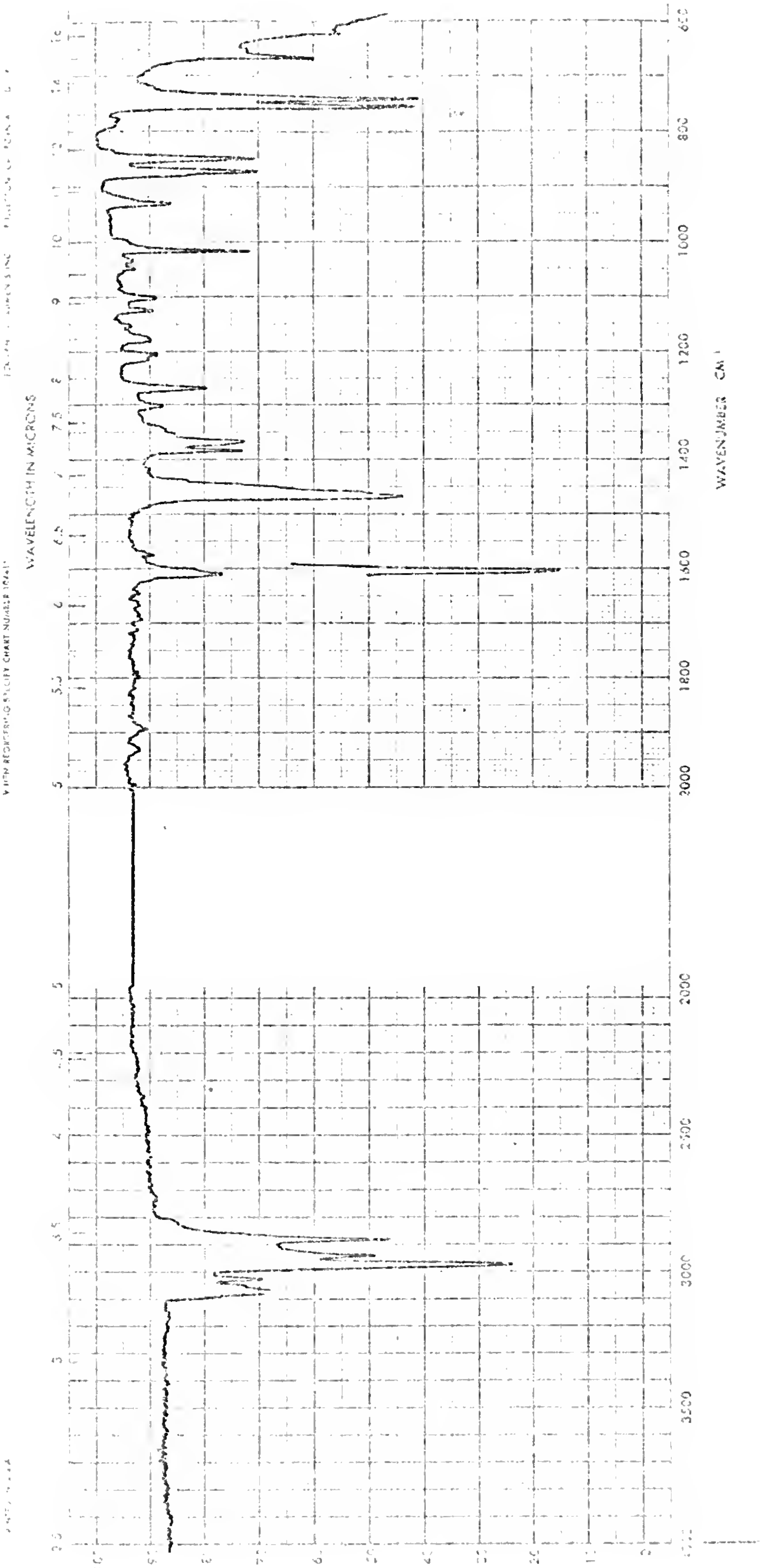


Figure A-35: Ir of 1-methyl-2-isopropylindene (63b)

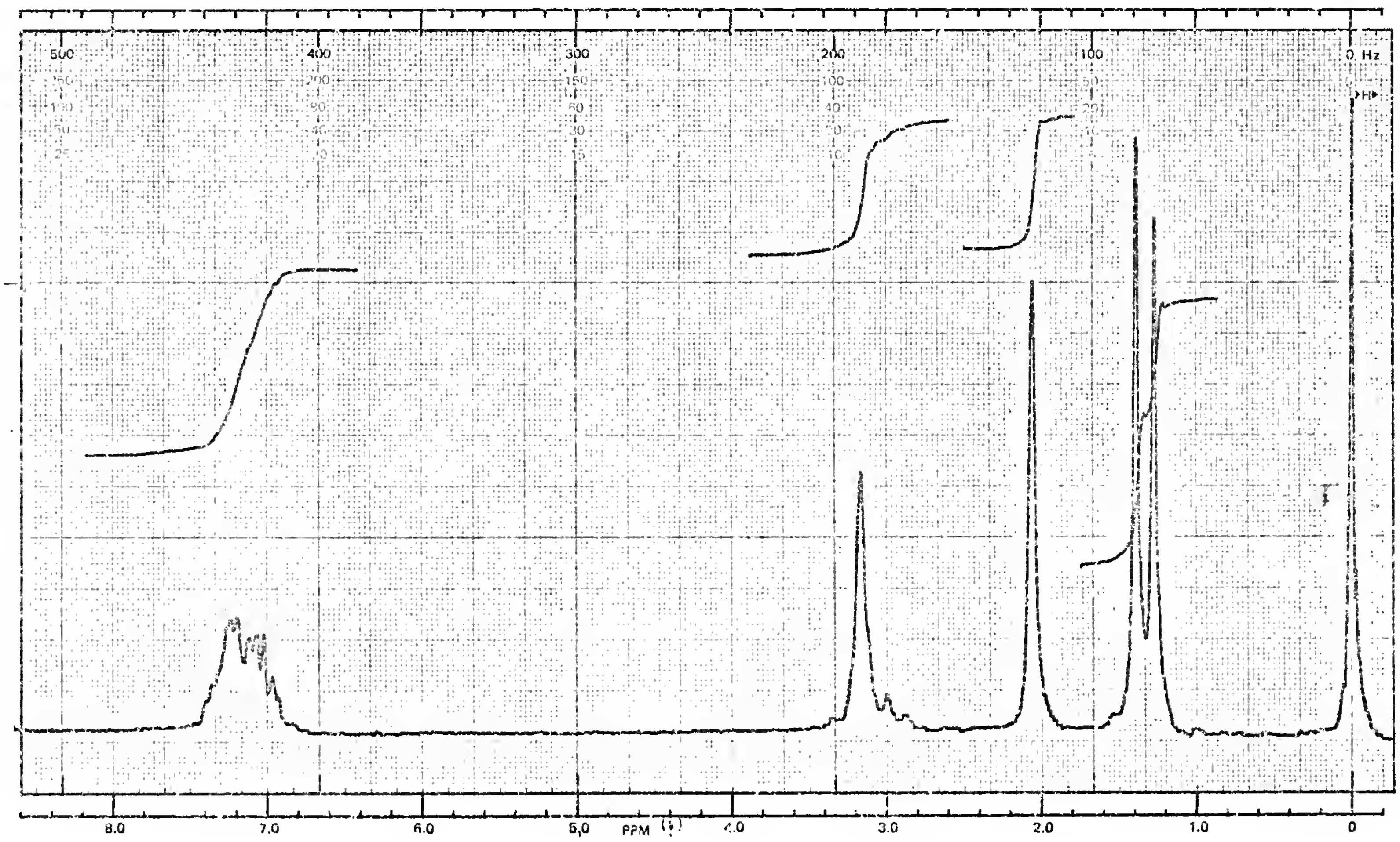


Figure A-36: Nmr of 2-methyl-3-isopropylindene (63c)

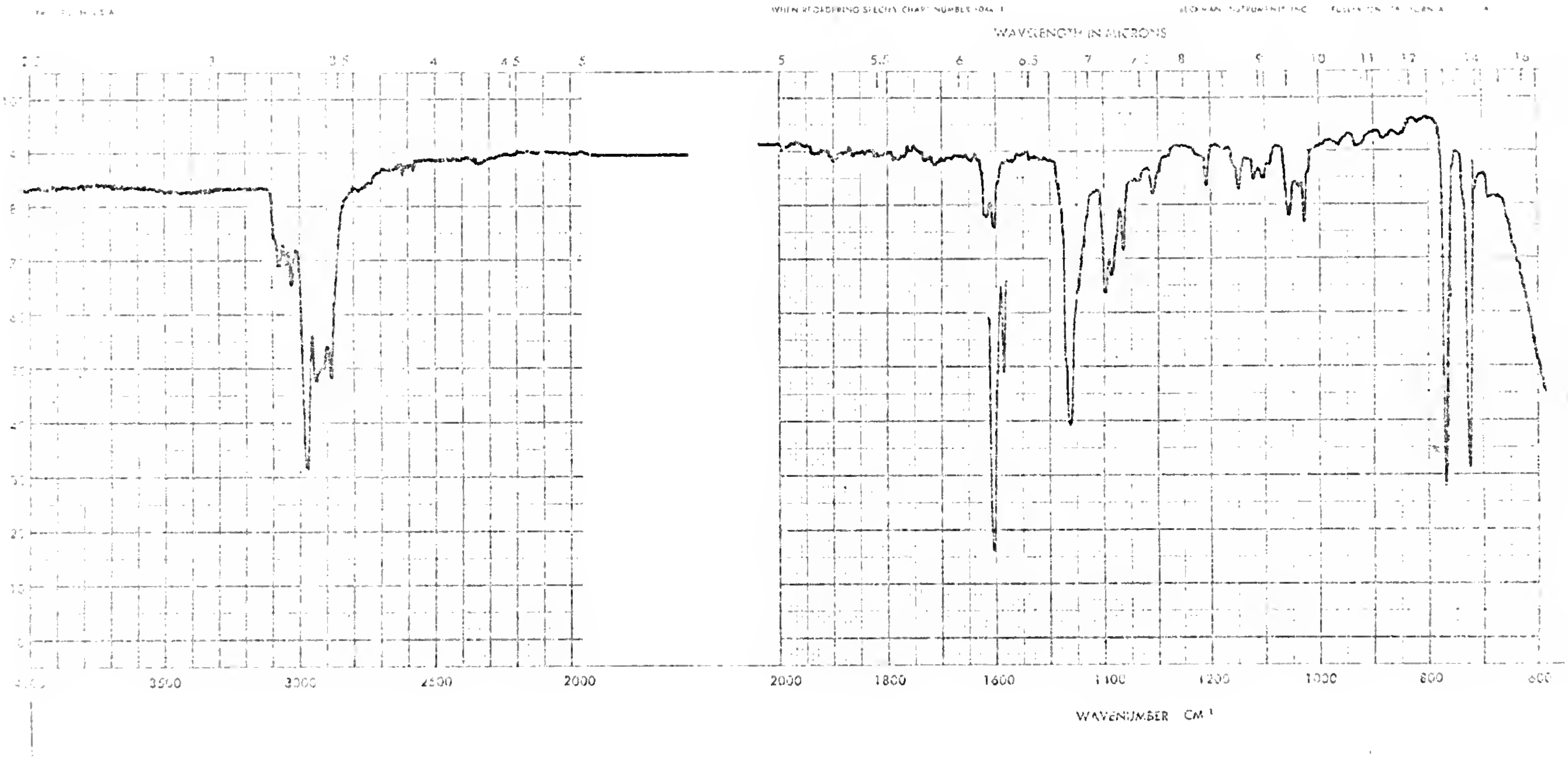


Figure A-37: Ir of 2-methyl-3-isopropylindene (63c)

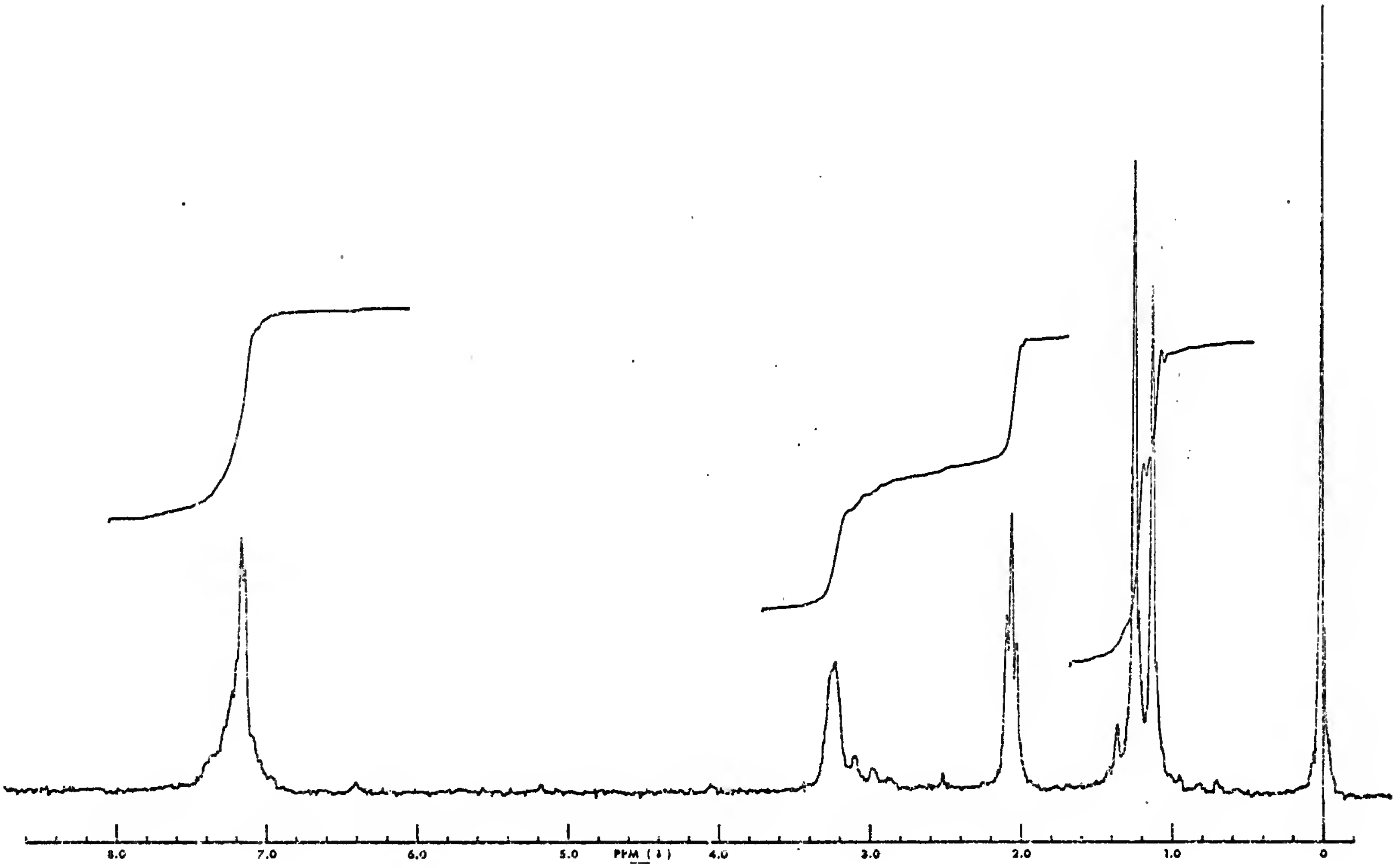


Figure A-38: Nmr of 2-isopropyl-3-methylindene (63d)

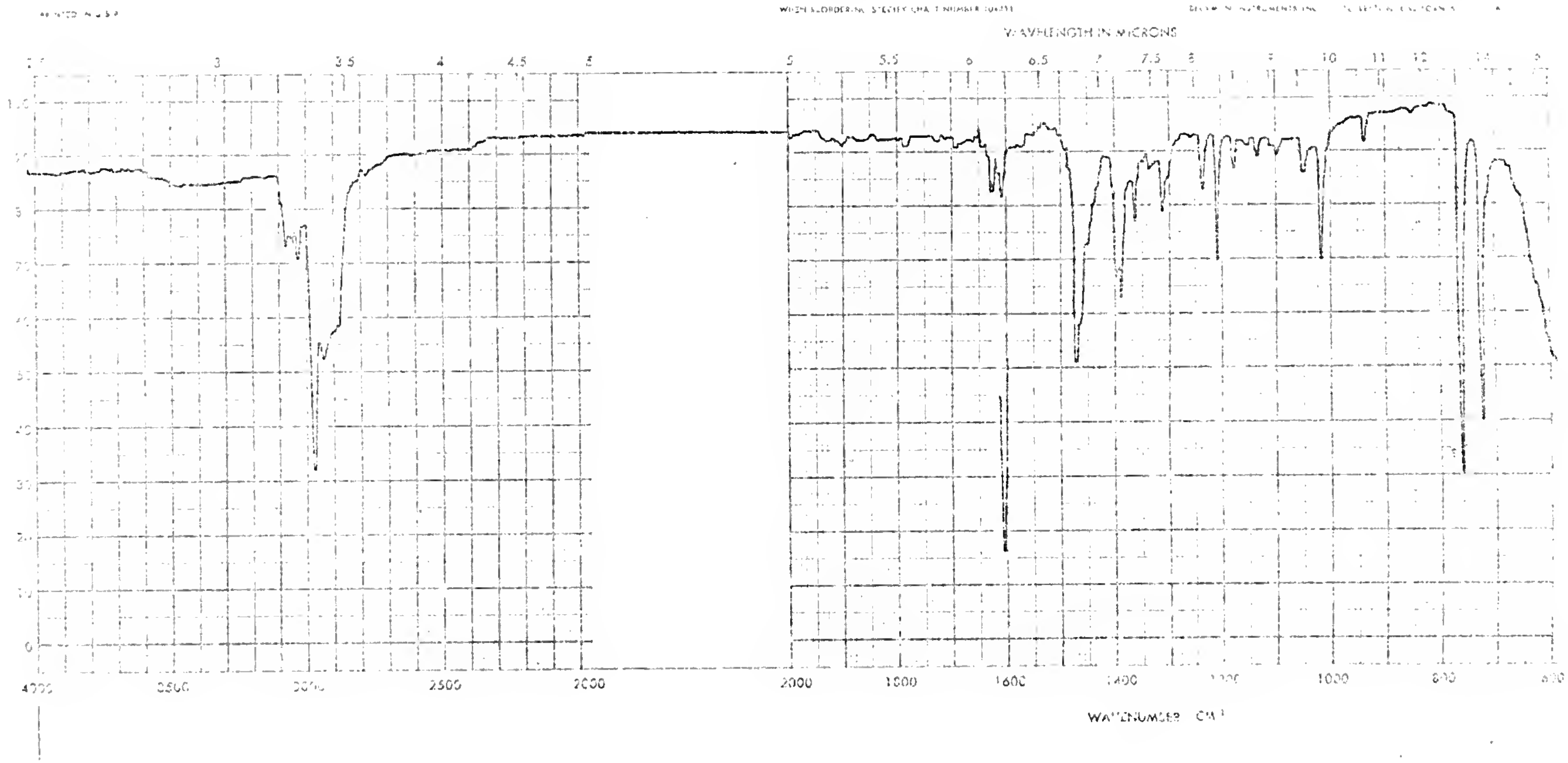


Figure A-39: Ir of 2-isopropyl-3-methylindene (63d)

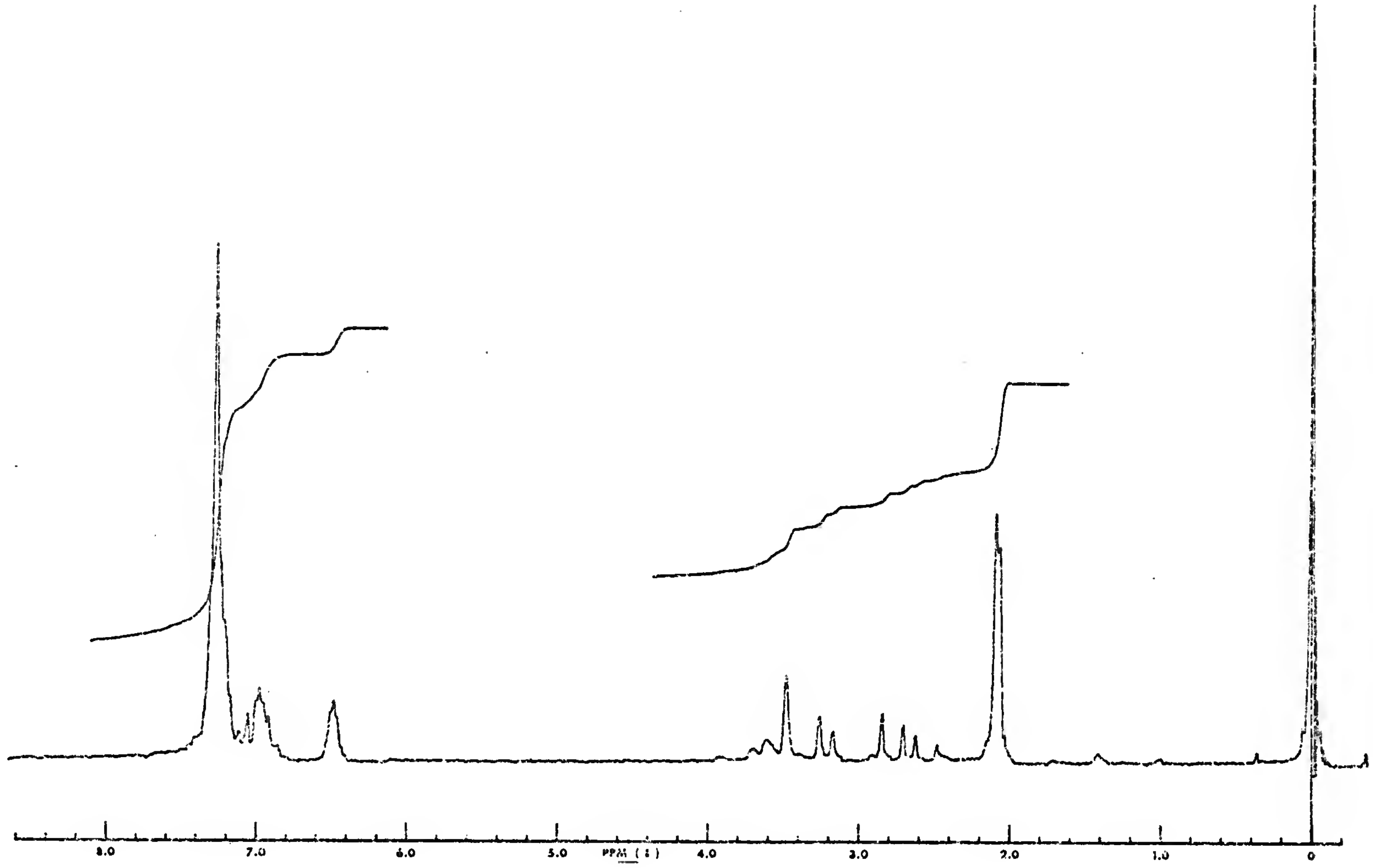


Figure A-40: Nmr of 1-benzyl-2-methylindene (<u>64a</u>)

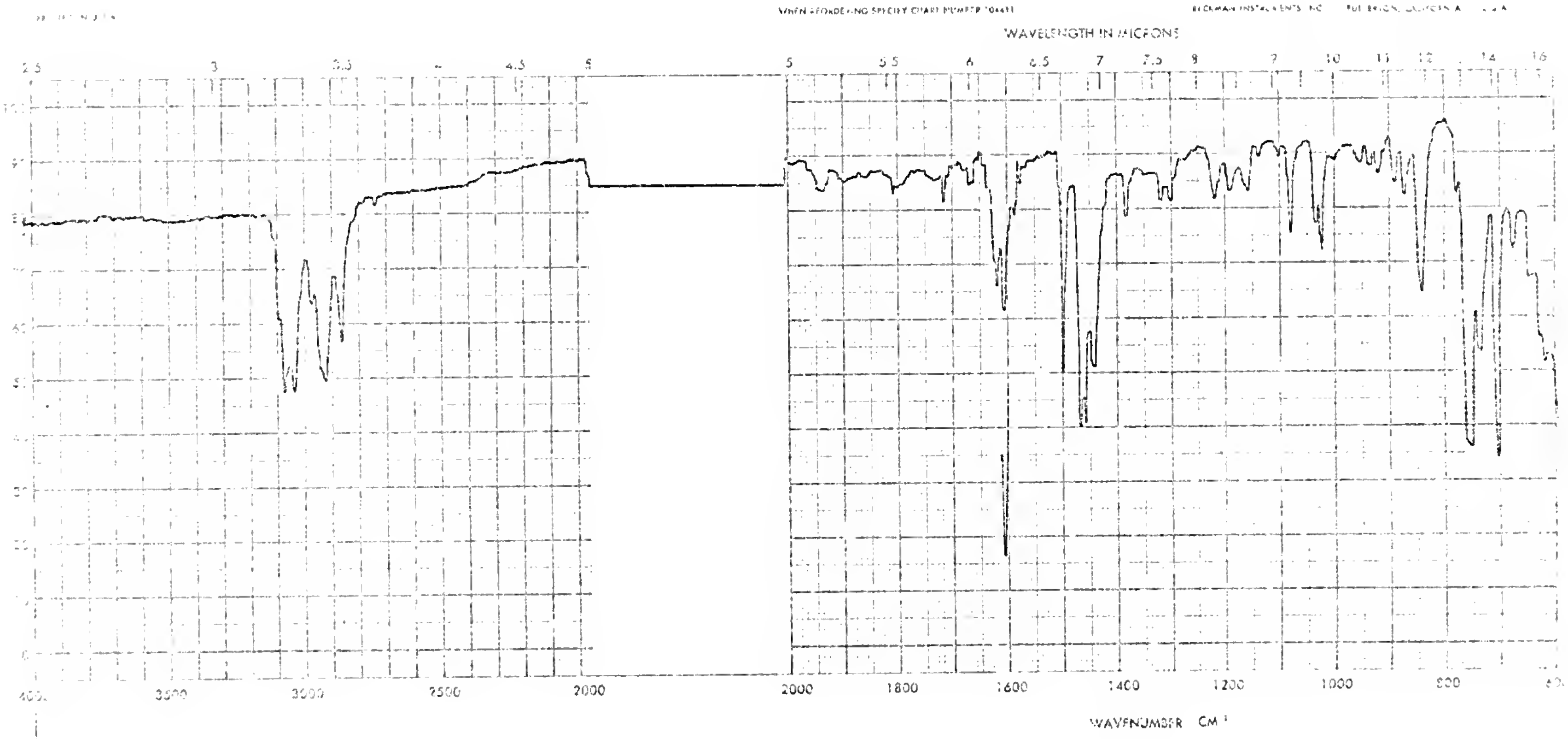


Figure A-41: Ir of 1-benzyl-2-methylindene (<u>64a</u>)

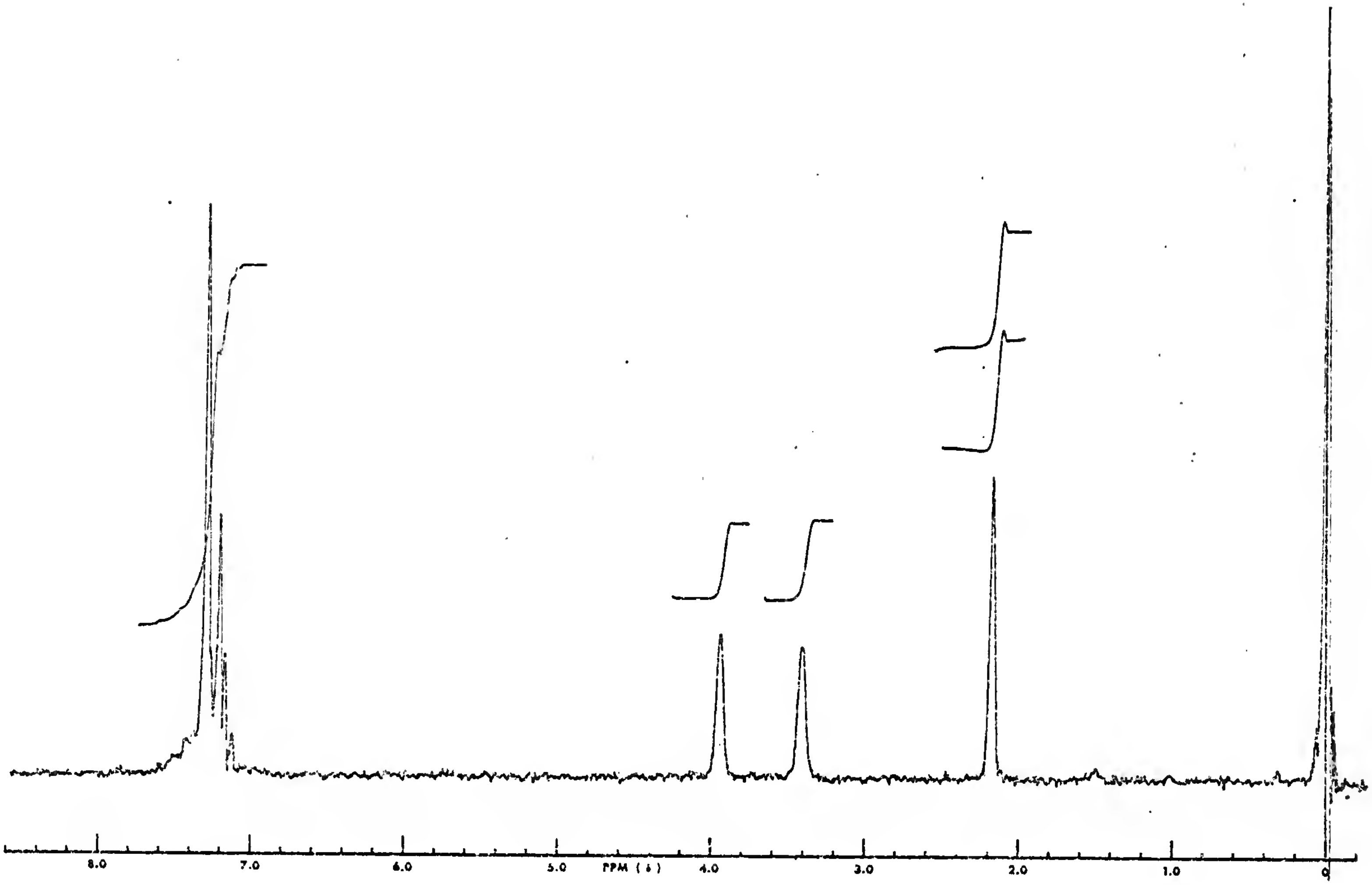


Figure A-42: Nmr of 2-methyl-3-benzylindene (<u>64c</u>)

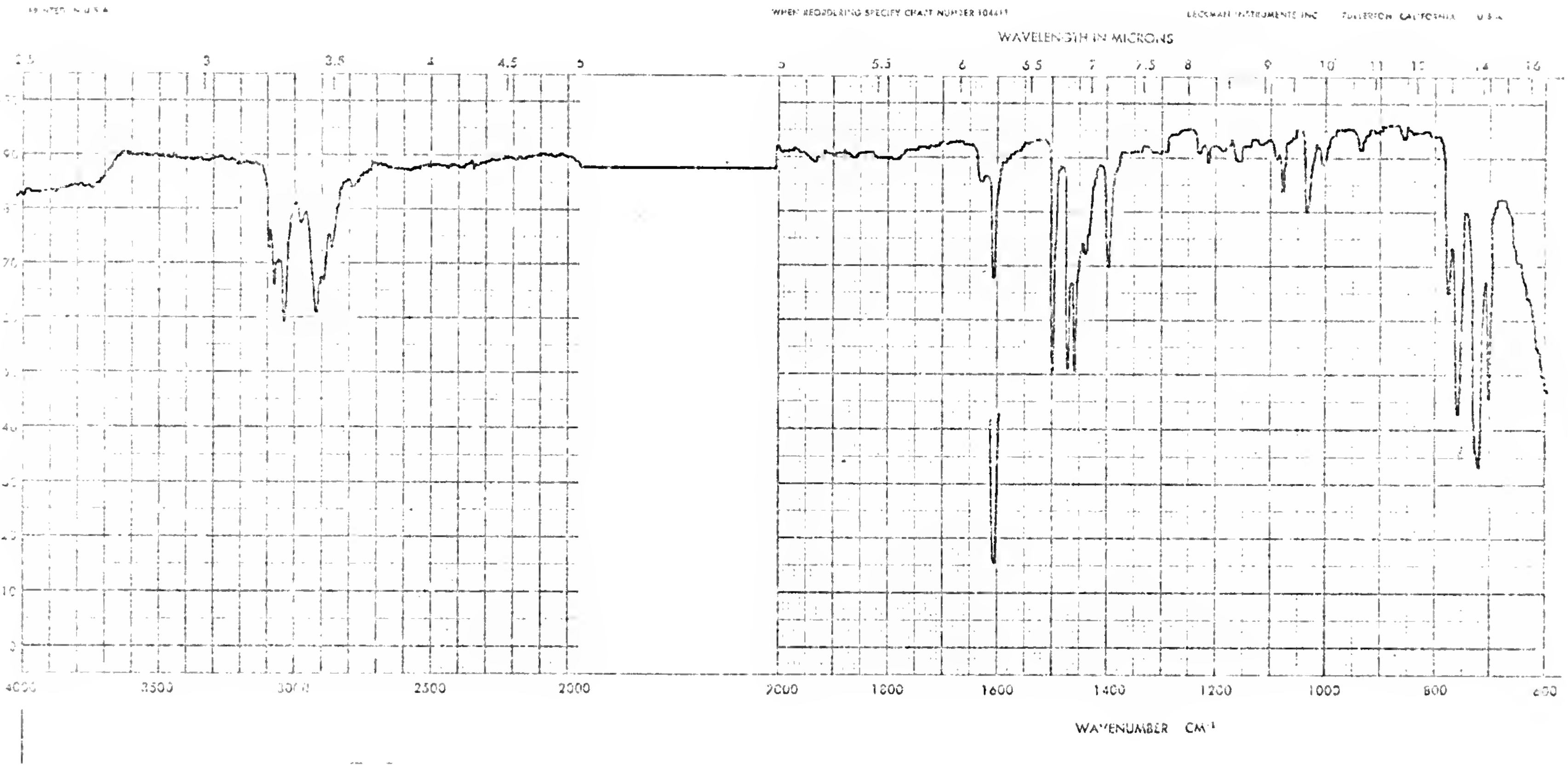


Figure A-43: Ir of 2-methyl-3-benzylindene (<u>64c</u>)

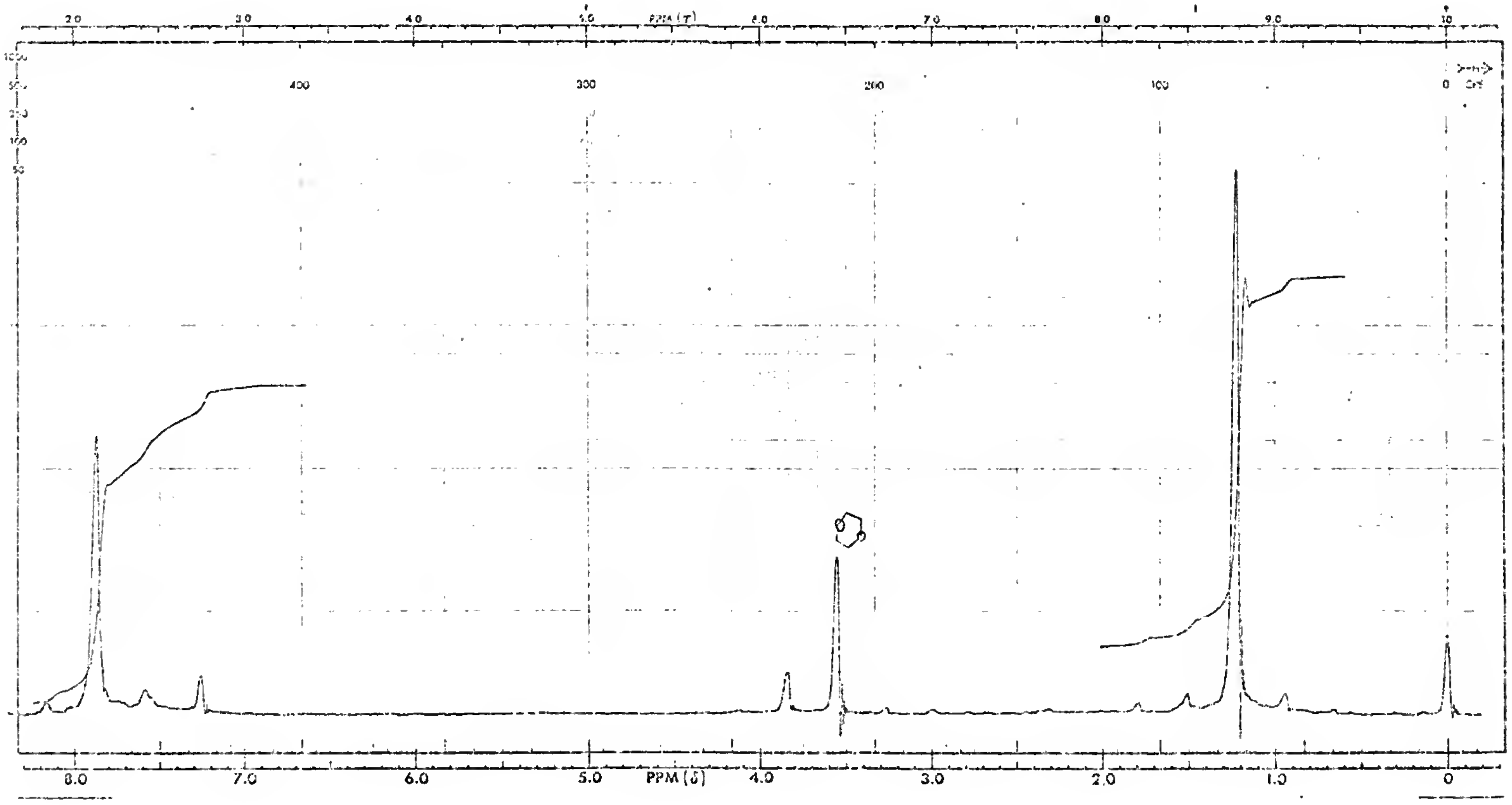


Figure A-44: Nmr of 2,2-dimethyl-1,3-indandione (47a)

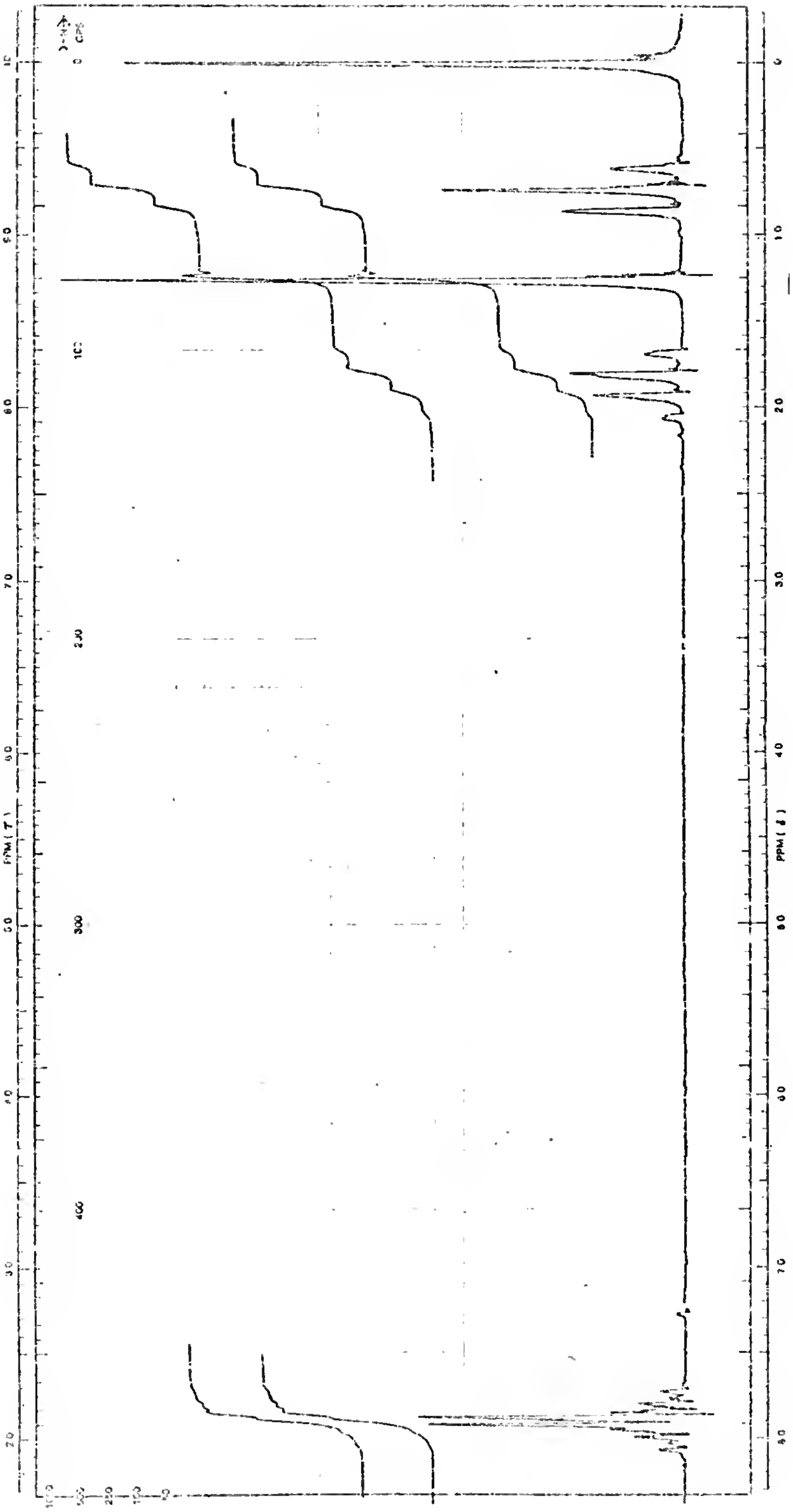


Figure A-45: Nmr of 2-ethyl-2-methyl-1,3-indandione (47b)

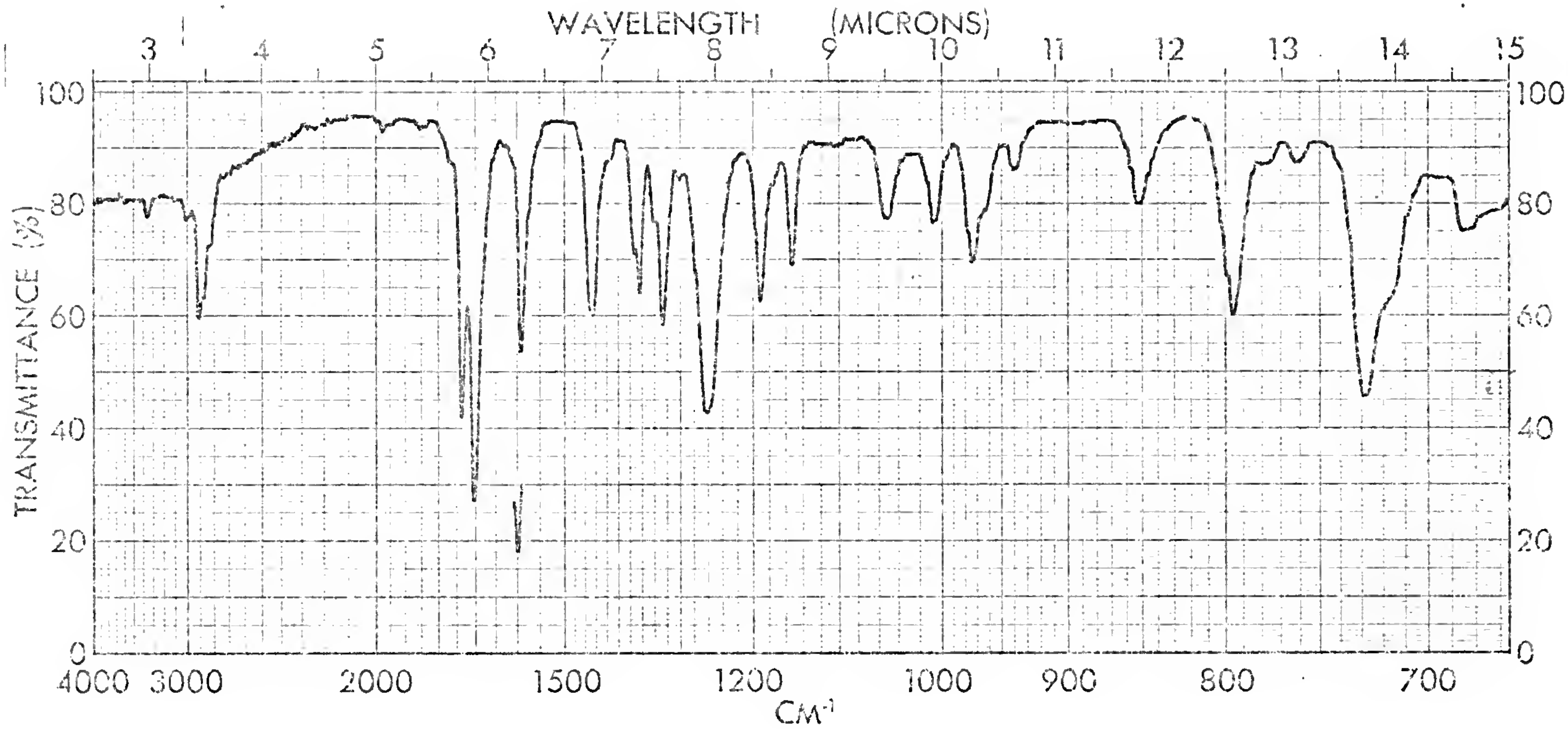


Figure A-46: Ir of 2-ethyl-2-methyl-1,3-indandione (47b)

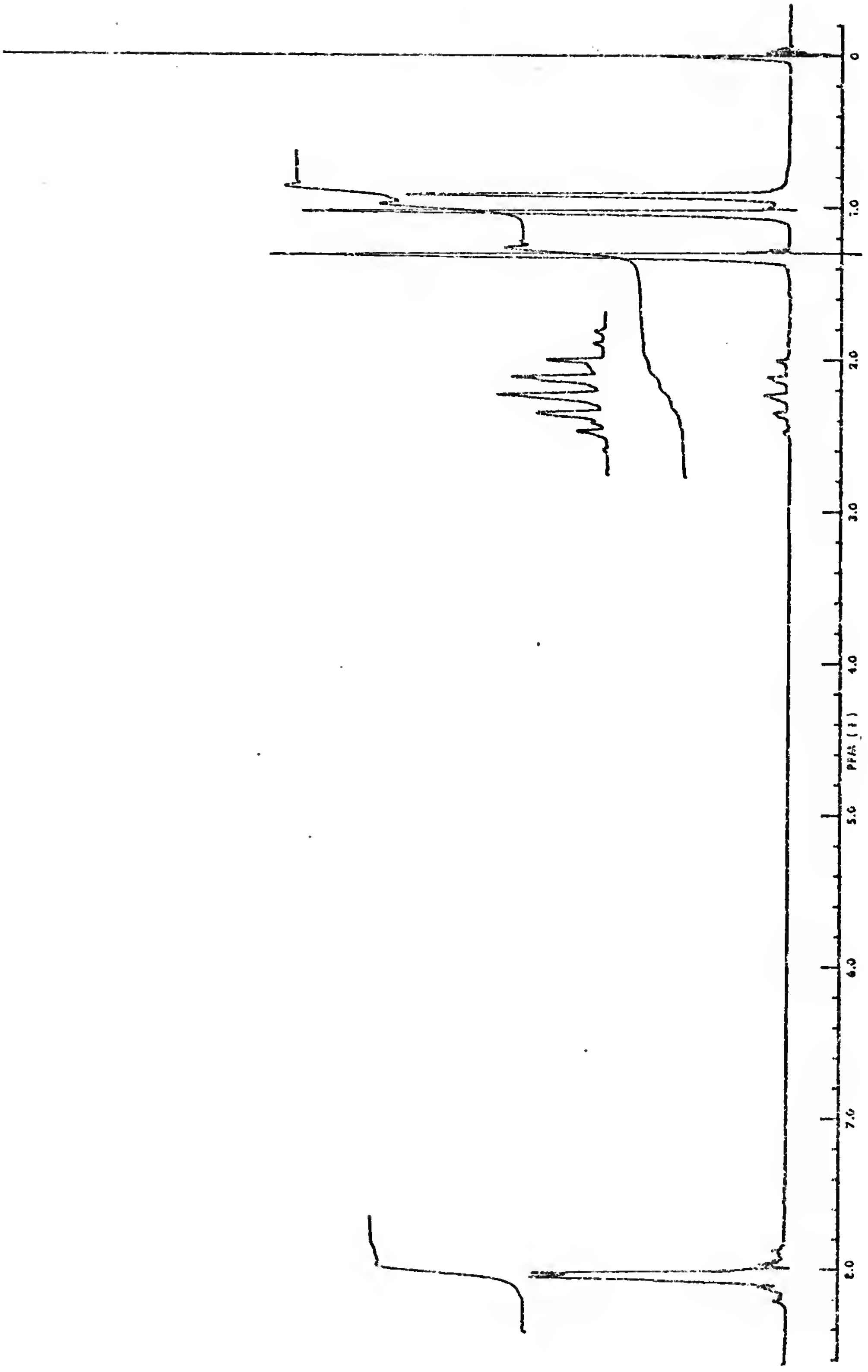


Figure A-47: Nmr of 2-isopropyl-2-methyl-1,3-indandione (<u>47d</u>)

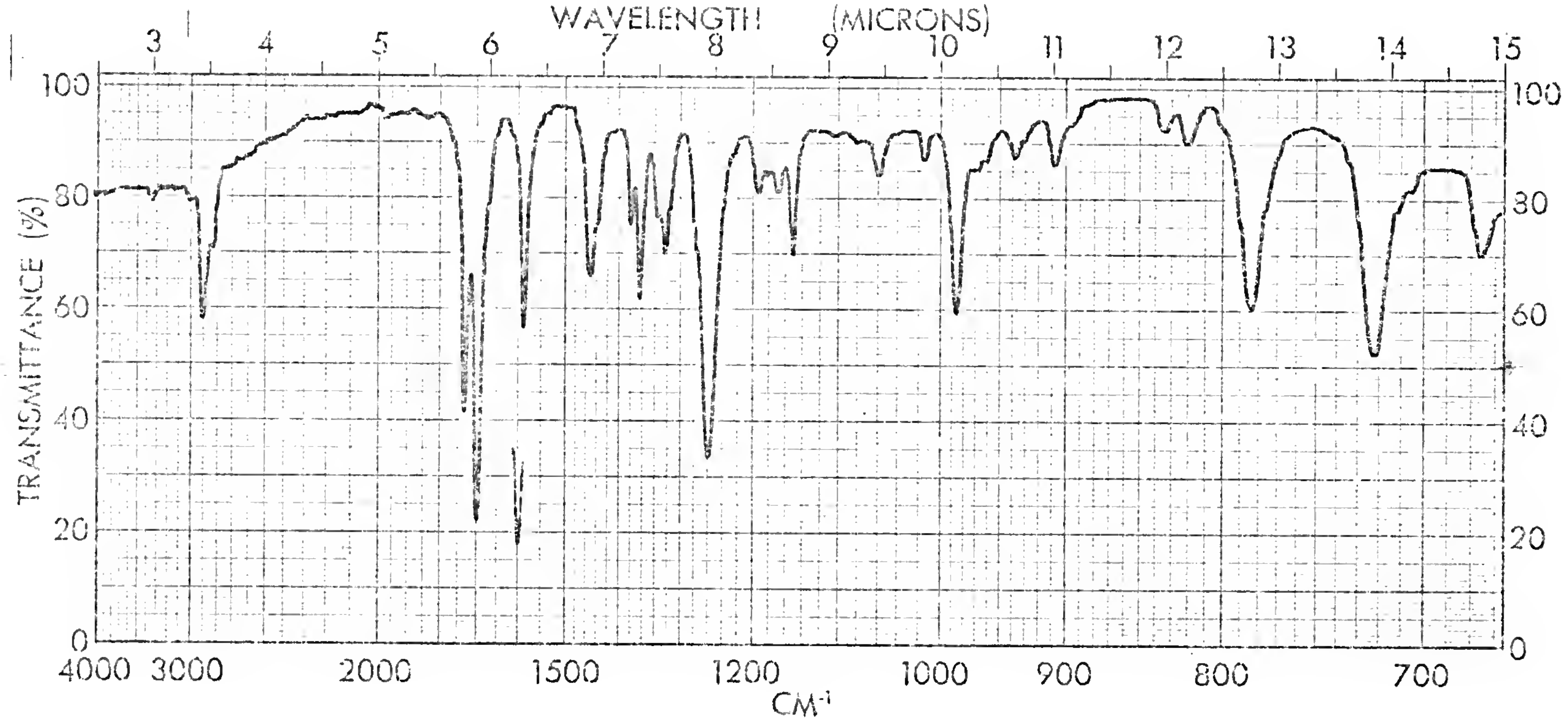


Figure A-48: Ir of 2-isopropyl-2-methyl-1,3-indandione (47d)

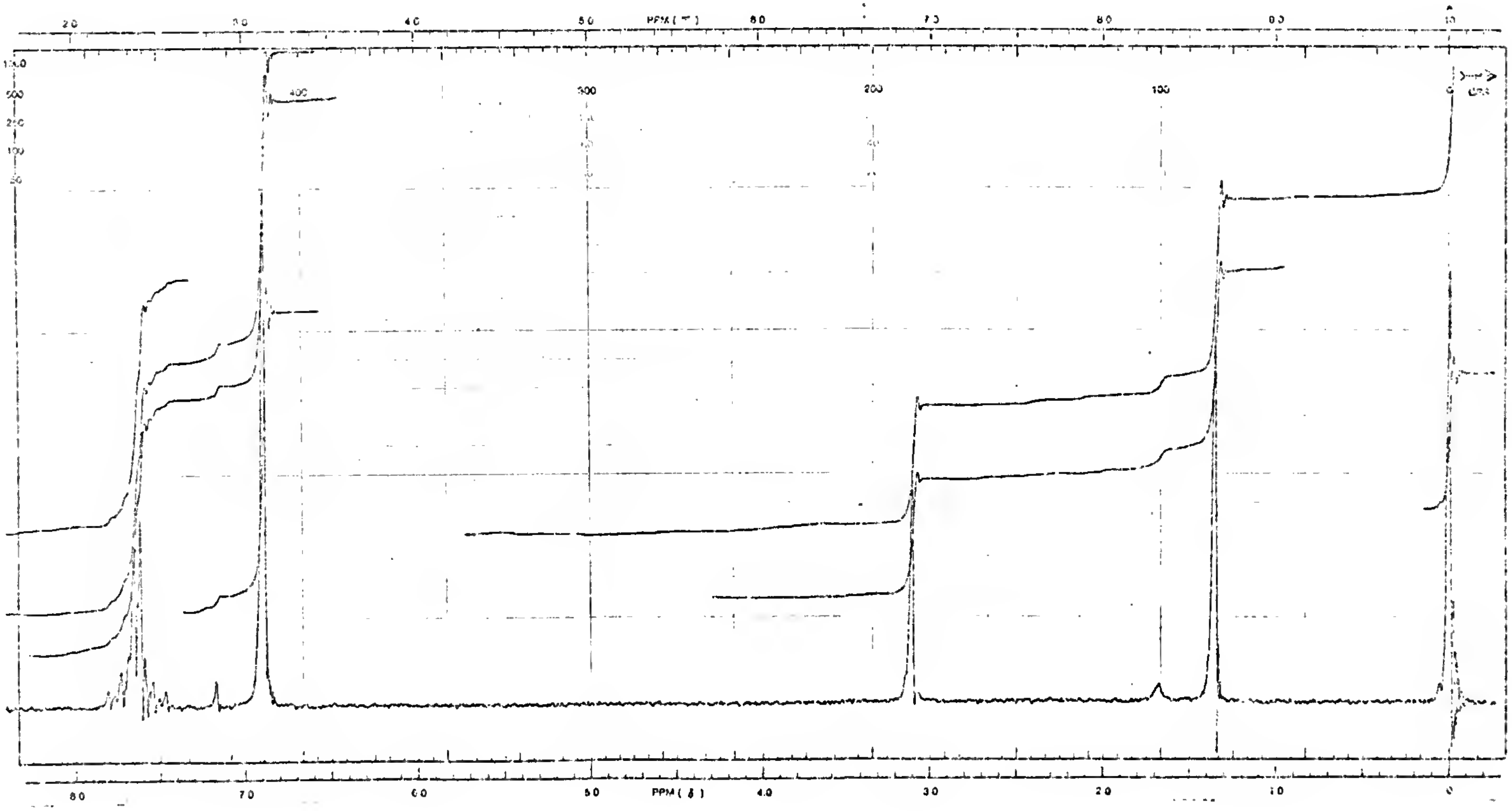


Figure A-49: Nmr of 2-benzyl-2-methyl-1,3-indandione (47e)

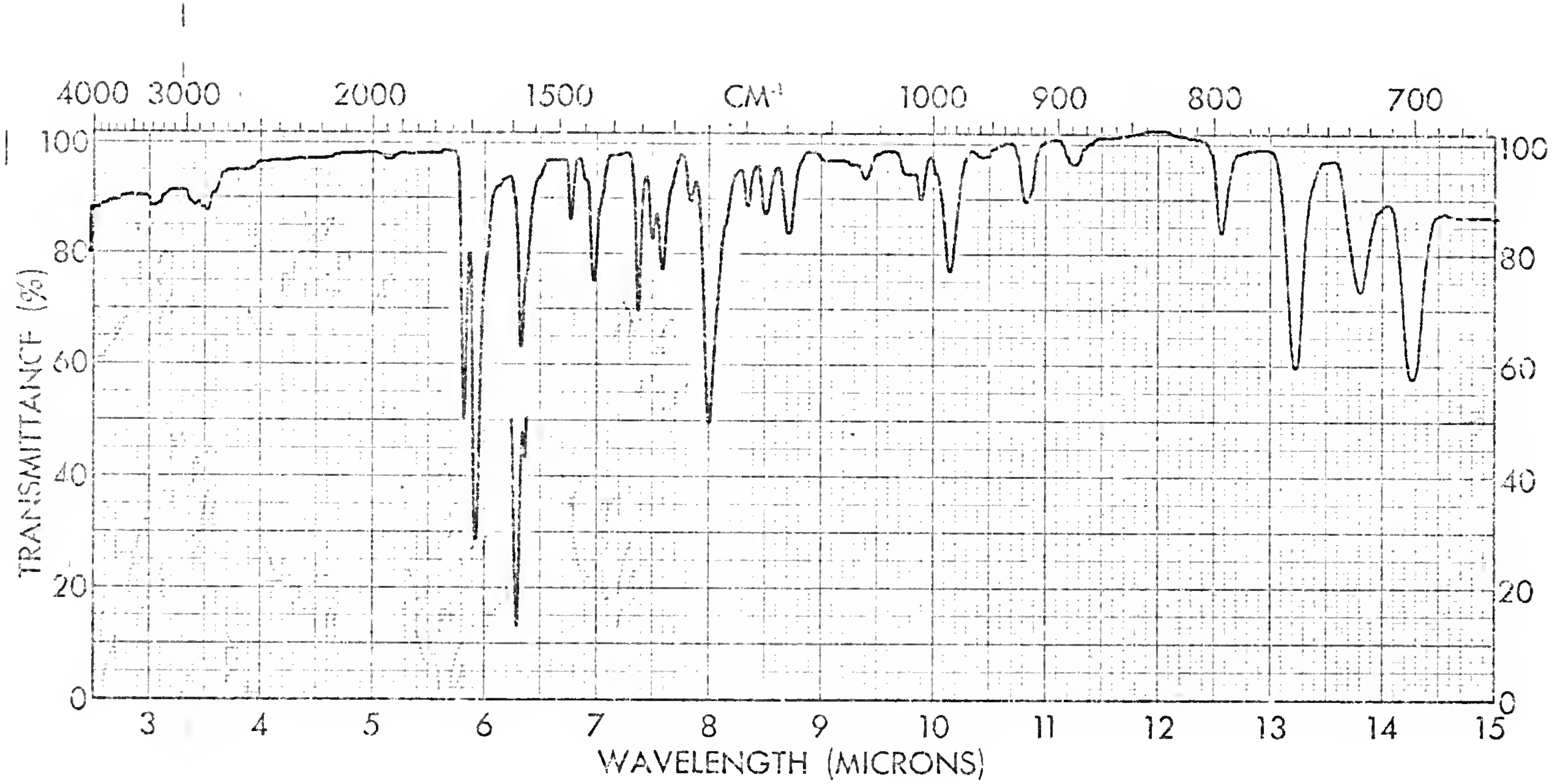


Figure A-50: Ir of 2-benzyl-2-methyl-1,3-indandione (<u>47e</u>)

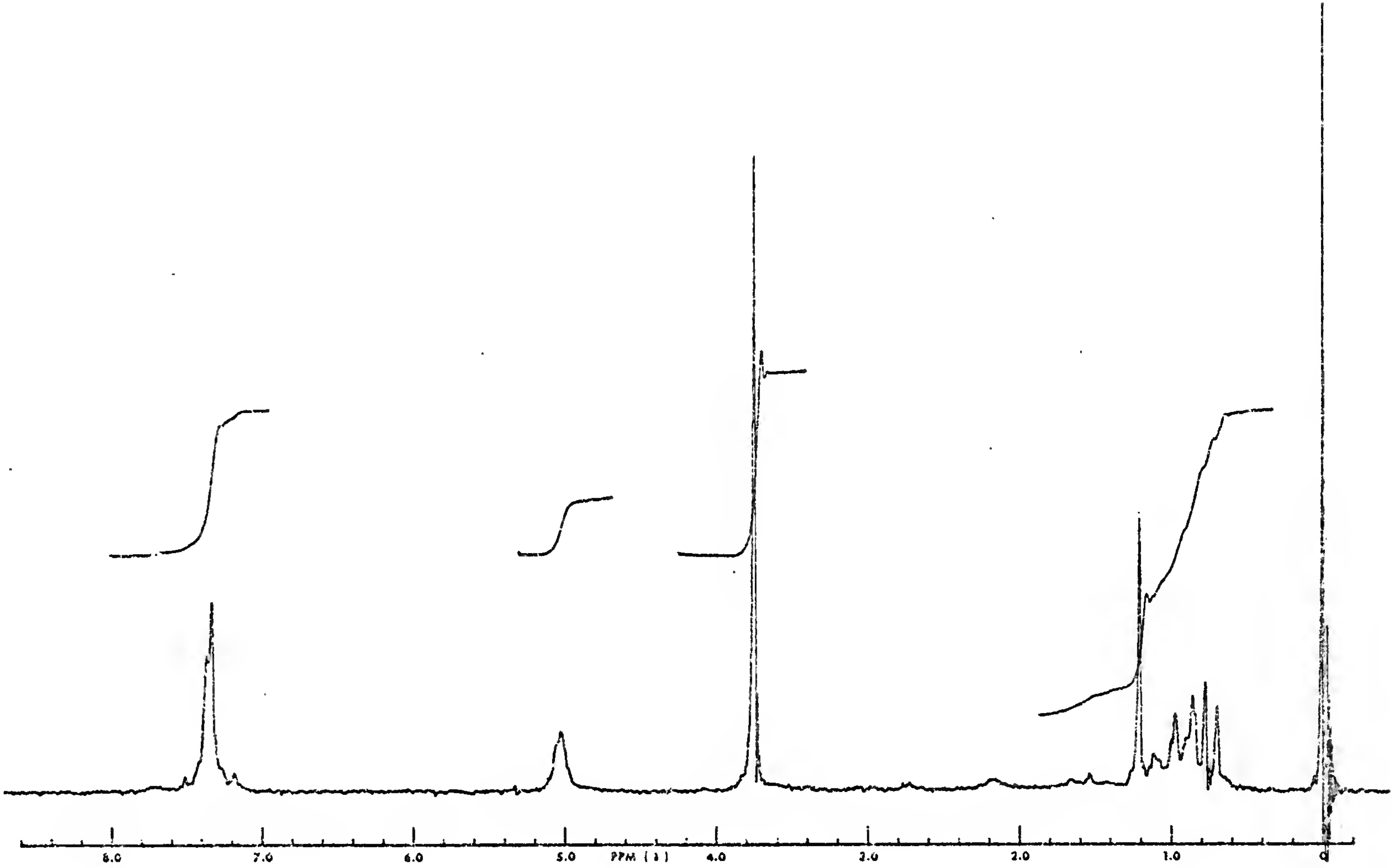


Figure A-51: Nmr of dimethyl 7-ethyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (51b)

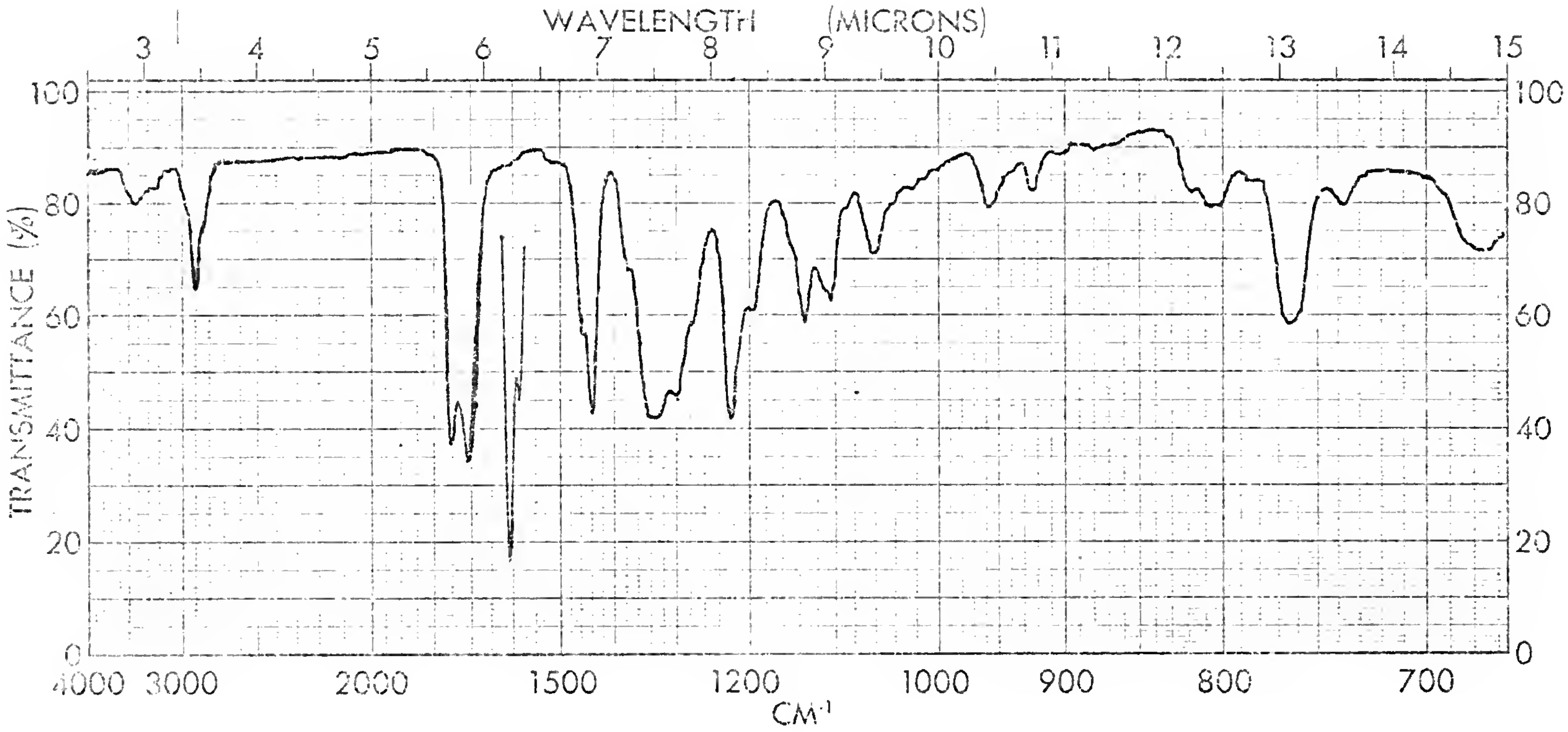


Figure A-52: Ir of dimethyl 7-ethyl-7-methyl-5,6-diaza-2,3-benzobicyclo(2.2.1)hept-2-ene-5,6-dicarboxylate (51b)

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BIOGRAPHICAL SKETCH

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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